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Red Cells Cut Crisis Severity in Sicklemia

Medical Tribune Report

PHILADELPHIA—An exploratory trial of prophylactic red cell transfusions in children with active sickle-cell anemia has reduced the severity and number of their crises, the National Medical Association was told here.

Severe crises were reduced to a "minimal point," and all patients were physically stronger throughout the three-and-a-half-year trial, it was reported by Dr. George W. Ward, Associate Professor of Pediatrics at Hahnemann Medical College. He spoke at the N.M.A.'s Pediatric Section.

The findings were made in 39 sickle-cell children who were placed on a program of regular packed red blood cell transfusions (PRBC) in order to determine if maintaining their blood hemoglobin level closer to 10 gm. would have beneficial effects on the frequency and severity of their crises.

The patient series consisted of 17 boys and 22 girls. Their blood hemoglobin levels were persistently between 6 and 8 Gm. per 100 ml., and all "had already had symptoms which were attributable to or associated with their sickle-cell anemia."

The investigations, Dr. Ward commented, sought to keep the blood hemoglobin level at about 9 Gm./100 ml. for the younger children and above 10 Gm./100 ml. for adolescents. When blood hemoglobin was found at or close to these thresholds during the patient's regular clinic visit, a specimen was drawn for cross-matching, and the patient returned within a few days for a PRBC transfusion. The transfusions were given in pairs, one day

Continued on page 24

Detoxifying Study Might Prove Aid In Pollution War

Medical Tribune Report

COLUMBIA, Mo.—The study of means to reinforce the body's detoxication system should be of value in dealing with the problem of environmental pollution, the fifth annual Conference on Trace Substances in Environmental Health was told here.

"In a situation in which an organism and a toxic chemical exist in the same locality, the organism can escape serious harm if either or both of two things happen," according to David J. Wagstaff, Ph.D., of the Department of Veterinary Physiology and Pharmacology at the University of Missouri.

"First, contact between organism and toxicant is avoided—i.e., toxicant concentration is kept low in the water, air, food, and other materials contacting the organism. Or, second, the organism detoxifies the toxicant. Both of these approaches should be fully researched and applied by our society."

Organisms and heavy metals or other
Continued on page 18

Ear Oximeter Tested



Experimental ear oximeter measures circulating blood's oxygen content by infrared absorption through ear. It was developed by NASA's Biomedical Applications Division.

World Cancer Registries Key To Environmental Patterns

Medical Tribune World Service

LYON, FRANCE—Scientists at the International Agency for Research on Cancer, a unit closely associated with the World Health Organization, are convinced that in world patterns of cancer incidence will be found new clues to the environmental causes of cancer. Dr. John Hingston, director of the agency, believes that approximately 80 per cent of all human cancers are caused or promoted by "exogenous stimuli."

"Take the role of cigarettes," Dr. Hingston told MEDICAL TRIBUNE. "It was only after 1945 that the epidemiological method was used for etiological studies. But by 1945 the evidence that was in was enough to convince me personally to stop smoking cigarettes."

The heart of the agency's global epidemiologic studies lies in a series of cancer registries for age-specific statistics—some

Second of four articles.

set up by the agency, others run by national governments, some by local governments.

'A Lot More Work' Necessary Before Human VD Vaccine Use

Medical Tribune Report

WASHINGTON—More than four years have gone by since the first successful experiments in immunizing animals against syphilis, but there is still "a lot of work to do before we can apply it to humans," a VD vaccine expert reported here.

Even in the rabbit experiments a practical dosage schedule has yet to be achieved, James N. Miller, Ph.D., acknowledged after a workshop session on gonorrhea and syphilis at the first International Congress of Immunology.

Dr. Miller, whose group at the University of California at Los Angeles is one of the very few to report an experimental vaccine success, said the current investigative difficulties include such basic matters as the inability to culture the syphilis-causing *Treponema pallidum* in vitro and the problem of storing the organisms (harvested from infected rabbits) without a loss of antigenicity.

He conceded that successful immunization of rabbits required "rather large doses over a long time" with *T. pallidum* organisms inactivated by gamma radiation from

a cobalt⁶⁰ source. The dosage—intravenous—was twice weekly over 37 weeks for a total of 3.7 billion organisms injected.

However, he said, the immunity conferred by this procedure appeared both complete and long-lasting, "for at least a year." Other immunization attempts using two or three times as many organisms over a shorter period than 37 weeks afforded less complete protection (an asymptomatic infection was sometimes detectable). A lesser degree of immunity also followed trials of vaccine produced by inactivating the organism with penicillin or simply with week-long refrigeration.

In the works now, he said, are trials of organisms quick-frozen and stored in liquid nitrogen. Also upcoming is a test dosage schedule of large numbers of organisms, injected intramuscularly three times at three-week intervals.

"First, we need more organisms, which is a production problem," said Dr. Miller. "Then we have to develop a practical dosage schedule that still confers immunity. And before a vaccine is ever made available."

Continued on page 18

Suppression of Permanent Abortion Record Urged

Medical Tribune World Service

HELSINKI—Applications for abortion should never be a subject of permanent record, Norway's director general of health services warned here.

"This is an essential precaution, which is already current practice in Norway, in case the request is not granted," Dr. Karl Evang told MEDICAL TRIBUNE. "If such records are destroyed, there is no danger that a child might one day discover it was not wanted."

Dr. Evang, who spoke to a World Health Organization working group meeting here about the administrative

aspects of providing services for induced abortion, pointed out that a service apparatus should be client-oriented. The procedure should not be too time-consuming, both from biologic (fetal growth) and psychologic aspects.

Invasion of a person's privacy must be as limited as possible, Dr. Evang added, and professional secrecy must be guaranteed. He also stressed the desirability of a decentralized administrative system to permit rapid decisions without lengthy referrals to higher authorities. If this leads to a certain degree of inequality, he said, this is a price one must pay.

Computer Generates Study Curriculum For Suicidology

Medical Tribune Report

CINCINNATI—The development and successful testing of a computer-generated curriculum for suicide studies that permits individual instructors to introduce a syllabus tailor-made for their students was reported here at the annual meeting of the American Association of Health Sciences here. The curriculum, developed by the National Institute of Mental Health, is a multidisciplinary mental health curriculum, said to be the first of its kind, has been piloted at a wide variety of institutions, among them three schools of medicine—Loyola University, St. Louis University, and the University of Texas Medical Branch at Galveston. In addition, a pilot program was also carried out at the National Naval Medical Center, Bethesda, Md.

The report on the curriculum and a demonstration of its workings were made to the meeting by Dr. Harvey L. P. Resnik, chief of the Center for Studies of Suicide Prevention of the National Institute of Mental Health; George R. Murray, Ph.D., vice-president of KMB Health Systems, Inc., Palo Alto, Calif.; and Barkley C. Hethorne, Ph.D., coordinator of education and training at the NIMH suicide studies center.

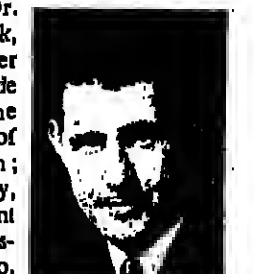
The Center for Studies of Suicide Prevention will maintain and operate the program. KMB Health Systems is under contract to the center to assist in the planning, development, and evaluation of the curriculum system.

Although suicide is a major public health problem—ranking 11th as a cause of death—its introduction into the curriculums for training the wide variety of professionals and volunteer workers who are likely to encounter the phenomenon has been spotty, Dr. Resnik declared.

He stressed that the stimulus to develop the computer-generated curriculum stemmed from the very variety of disciplines requiring such knowledge. The target groups for such information, he noted, range from schools of medicine, nursing, social work, and theology to police training programs and community courses for volunteer workers.

The work of putting the curriculum together began with two rounds of sessions with some 50 suicide specialists drawn from the many disciplines concerned. The

Continued on page 23



DR. RESNIK

Late Regression Found in Therapy For Parkinsonism

Medical Tribune World Service

ROME—A one-year follow-up of amantadine treatment in 44 parkinsonism patients showed a "marked regression" in the improvement that had been noted during the first six months of therapy. Dr. G. Dalle Ore, of the Hospital Institutes of Verona, told the De Angeli Institute Convention on Amantadine.

"The regression is most evident in the case of the symptoms that benefit most from the treatment—rigidity and akinesia," he said.

In the first six months of a daily dosage of 250 to 300 mg., there was a "notable reduction in rigidity." Twenty-one patients showed excellent results, 12 good results, and one fair improvement. Six showed no change, and four worsened.

Daily Life Improved

The first six months also showed a marked improvement in the daily life of the patients. Dr. Dalle Ore reported. Eight patients achieved complete autonomy, 30 were self-sufficient, six needed partial aid, and none needed complete assistance.

"At 12 months the picture is less comforting," he said. "The number of completely autonomous cases has fallen to three, the self-sufficient to 24, and 17 patients need outside help. Of the latter, six need complete assistance."

"He commented that amantadine works more effectively and is better absorbed than levodopa in the long-term treatment of parkinsonism. The major therapeutic efficiency of levodopa, considering that in patients treated with this drug, after a year of treatment it is possible to demonstrate major improvement in akinesia, rigidity, and, above all, in tremors."

Coauthors were A. Bricolo, P. Buffatli, A. Bazzan, and C. Mazza.

Ape Gets Marrow Graft



Immunologic deficiency diseases are under study at the Radiobiological Institute, an animal research center, in Rijswijk, the Netherlands. Above, a bone marrow transplant on a monkey.

Medical Schools Will Be Added To State Universities in Japan

Medical Tribune World Service

TOKYO—Japan's Ministry of Education has launched a plan to increase enrollment in state medical schools by 1,500 over a 10-year period beginning in 1972. Medical schools will be opened in three state universities, Education Minister Michita Sekata announced.

The announcement follows growing public concern over the shortage of facilities for state training in medicine. Competition is so keen that several hundred students compete for a place available in the state medical schools.

This has exacerbated the shortage of doctors, particularly in rural areas, and resulted in an overdependence on Japan's 13 private medical schools, where tuition is high. Today a donation of up to \$28,000 is often required for enrollment at a private medical school.

Regimen Advanced to Cut Loss Of Ability in Child Dystrophy

Medical Tribune World Service

JANSKE LAZNE, CZECHOSLOVAKIA—Loss of functional capacities can be delayed for more than five years in children with rapidly evolving Duchenne muscle dystrophy by a regimen including a vasodilator drug, hat baths, massage, and passive muscle stretching, providing the diagnosis is made early, according to Dr. J. Demos, director of research, Institut de Pathologie Maléculaire, University of Paris. These results constitute new evidence for the microcirculatory origin of the disease, he told the second Conference on Myopathies here.

Values in Newborns Compared

While nondystrophic newborns have serum creatine kinase values of not more than 445 I.U., with activity decreasing in the first years of life, dystrophic newborn boys were found by Dr. Demos' institute to have values between 755 and 4,482 I.U., increasing thereafter up to the age of three. The SCK level can thus be used to diagnose the disease in the first few months of life.

The daily program recommended by Dr. Demos includes 60-120 mg. of (p-hydroxyphenyl)butylaminoethanol, a peripheral vasodilator, daily; a half-hour morning hot bath (38° C., or 100° F.), followed by manual massage of shoulder, arm, buttock, thigh, legs, and back muscles; passive stretching of muscles of the foot, knee, and hip; use of splints at night; and no active muscular re-education, climbing stairs, or repeated standing.

This approach has been used for eight

Dr. Demos said, circulatory troubles in dystrophic patients have been observed by a number of authors. In his experience, 60 per cent of dystrophic patients have cerebral disturbances. Of the 100 child patients described, 95 had significant growth retardation.

Observations in apparently normal carriers, he said, suggest that these circulatory abnormalities are not caused by muscle lesion but by the genetic mutation responsible for the disease. Mothers known to carry dystrophy because of an X-chromosome defect have Reynaud's disease in 50 per cent of cases, an often significant decrease of peripheral circulation time, and a positive and significant correlation between circulation time and serum aldolase and SCK levels.

Finally, Dr. Demos reported, his institute has shown, by electrophoresis of blood platelet extracts, the existence of an enzyme that catalyzes the oxidation of epinephrine into adrenochrome and of DOPA into melanin. This enzyme, known as diphenol oxidase, displays abnormal behavior both in the dystrophic subject and in carriers, and this "opens the way to a new pathogenic study of the disease at the molecular level in addition to the systemic level where it has been concentrated until now."

Psychosis Incidence High In Australian Workers

MELBOURNE, AUSTRALIA—Evidence from animal and human experiments in the treatment of deep burns and other types of graft suggests that skin from uremic donors provokes a less vigorous immune rejection response than normal skin. This may be due to antigen masking by substances produced in uremia.

Uremic Donor Skin Preferred In Burn Grafts

Medical Tribune World Service

MELBOURNE, AUSTRALIA—Evidence from animal and human experiments in the treatment of deep burns and other types of graft suggests that skin from uremic donors provokes a less vigorous immune rejection response than normal skin. This may be due to antigen masking by substances produced in uremia.

This hypothesis was put forward at the fifth International Congress of Plastic and Reconstructive Surgery here by Drs. H. Pierer and H. Fladerer, Department of Surgery, University of Graz, Austria.

Following animal experimentation on rabbits, Dr. Pierer reported, a study was made of four human patients aged from 56 to 80, on whom small test strips of uremic skin were applied during the autoplasmic covering of small skin defects and the time of the beginning of rejection was determined. Simultaneously transplanted nonuremic skin sections survived eight, 10, 13, and 14 days in this group. In contrast, survival time of uremic skin homographs applied as small test strips were 20, 23, 29, and 32 days. Again the results were highly significant statistically.

Cadaver Skin Use Reported

Dr. Pierer next reported the use of cadaver uremic skin in burn cases. The research group uses only cadaver skin to fulfill requirements for homologous skin for covering severe burns. This skin qualifies as uremic only when the cause of death was in fact uremia or when a residual nitrogen over 100 mg. per 100 ml. had existed for an extended period. The split skin is removed under sterile conditions and stored at 4° C. for not more than 14 days. Blood group compatibility was not determined and tissue typing was not performed in any case before death.

Six patients ranging in age from two to 61 years with severe burns over 30 per cent to 60 per cent of the body surface were investigated. It was noted that rejection began relatively uniformly after approximately four weeks without adverse effect on the general condition and without temperature increase. Rejection lasted at least one week.

The decrease in the wound surface was striking in all cases with alternating arrangements of auto- and homologous grafts. The saving of autologous skin here amounted to more than half of that originally required. The authors concluded that the uremic condition of the skin helped the rejection to proceed very slowly and with very slight histologic reaction.

The nature of the changes in the graft caused by uremia remains unexplained. A reasonable assumption, the authors stated, would be a reduced antigenicity, possibly because of masking of antigen caused by substances produced in uremia.

Physician Aides to Be Trained

BIRMINGHAM, ALA.—A program to train physicians' assistants in diabetes has been launched here by the University of Alabama and the School of Community and Allied Health Resources.

Believed to be the first of its kind, the two-year program will train students to relieve diabetologists of routine duties, take patient histories, do physical exams, and provide routine patient analyses.

Now I am at a loss to know whether it be my hare's foot which is my preservation; for I never had a fit of the colic since I wore it, or whether it be my taking of a pill of turpentine every morning.

Samuel Pepys (1633-1703)
Diary, March 26, 1665

Occluded Artery Repaired



Almost total occlusion of left internal carotid artery is seen in angiogram.



In same patient, one year postoperatively, the left internal carotid artery.

Reimplantation of Carotid Advised In Children With Blocked Arteries

Medical Tribune Report

PHILADELPHIA—Reimplantation of the internal carotid artery to a lower level in the common carotid was recommended here as the preferred treatment for children suffering from obstructive elongation and kinking of the internal carotid arteries.

Drs. Charles M. Parrish and James P. Byrne, Jr., of the University of Utah College of Medicine, reported their experience with five children suffering from this malformation to a meeting here of the Society for Vascular Surgery. Four of the children were treated surgically; the fifth, a six-year-old girl with only moderate tortuosity of the left internal carotid, has been maintained on an anticoagulant.

The physicians observed that, while the abscission of cerebral blood flow secondary to the defect could result in permanent neurologic deficits, convulsive disorders, and transient ischemic attacks, the entity was less frequently recognized in children than in adults.

A range of symptoms appeared in the children whose cases they reviewed:

- In the first case, a five-year-old boy experienced malaise and headache 24 hours before admission and developed status epilepticus 45 minutes before admission. He was mildly febrile, comatose, and cyanotic.

with shallow respiration and right hemiparesis.

- In the second case, a five-year-old boy developed progressive aphasia and right hemiparesis. He was afebrile.

- The third patient, a 12-year-old boy, had a history of four nocturnal generalized convulsions in 10 months, each followed by hemiparesis and dysarthria that completely cleared in 30 minutes.

- The fourth, a four-year-old boy, was admitted with right hemiparesis. He was afebrile but showed right central facial paralysis and aphasic aphasia.

For diagnostic purposes, percutaneous angiography was performed through a common femoral artery under general anesthesia.

"Because of the small-sized vessels, shortening of the common carotid artery by segmental resection and end-to-end anastomosis was used in case 4," the investigators reported.

Otherwise, after straightening of the internal carotids, "the origin of the internal carotid artery was divided by a diagonal incision," they said. "The opening in the common carotid was closed. The internal carotid was reimplanted 2 to 4 cm. down the common carotid by an end-to-side anastomosis."

Investigators Say Sugar Has Ability To Stimulate Fat Production in Body

Medical Tribune Report

UPTON, N.Y.—Investigators at Brookhaven National Laboratory here have turned up evidence that sugar has the ability to stimulate production of fat in the body in some way apart from its caloric content in the diet.

The stimulation of fat production by sugar appears to be particularly great in women taking oral contraceptives, according to a team of investigators headed by Dr. Winton W. Shreeve.

Ten female and two male patients, most of whom were obese, were first put on a high-sugar-low-starch diet (9:1 ratio), then on a high-sugar-low-starch diet (9:1). Both diets contained the same amount of calories (about 2,500 daily) and the same total carbohydrate (about 60 per cent of total calories).

After seven to 10 days on each diet the patient was given by mouth about 100 Gm. of dissolved sugar labeled with carbon-14. Blood samples were then taken at one, three, six, and 12 hours after each "meal" of the labeled sugar. The blood specimens were fractionated to separate out the serum lipids, which were then analyzed in a scintillation counter to determine the C¹⁴ content.

In each case the concentration of C¹⁴ in serum triglycerides attained a peak during the three-to-six-hour period and then declined. After the high-sugar diet, however, the percentage of the labeled sugar converted to triglycerides was two to five times greater than in the same patients when on the low-sugar diet.

As expected from earlier studies, the concentration of the total serum triglycer-

ides (labeled and unlabeled) also sometimes increased after the high-sugar diet, but not as much or as often as the increase in C¹⁴ content. The findings support the concept of increased fermentation of fat with possibly increased turnover and transfer to other tissues from the blood, according to Dr. Shreeve.

Dr. Shreeve and his colleagues also studied the effect of the high-sugar diet on insulin production and found that during the first hour or two after taking the test sugar by mouth there was, on the average, 15 per cent more insulin in the blood when on the high-sugar than when on the high-starch diet.

Other members of the research team were Drs. Ching-Hui Wu, Mitsuri Hoshi, and Ryukichi Kikkawa.

Panel Will Appraise Malpractice Actions Begun in New York

Medical Tribune Report

NEW YORK—All medical malpractice suits brought against physicians and hospitals before the New York State Supreme Court in Manhattan, beginning with the fall term, will first be heard by a three-member mediation panel, Presiding Justice Harold A. Stevens, of the Appellate Division, First Department, announced.

Each panel will consist of a Supreme Court justice, a lawyer, and a physician, and its aim will be to arrive at an amicable, voluntary disposition of the case, thus avoiding lengthy trials, especially in cases concerning highly technical matters, and relieving crowded court calendars, Justice Stevens explained.

Parties appearing before a panel may be represented by counsel, but he emphasized that the hearings will be informal, that no stenographic record will be kept, and that, if the case proceeds to trial, the following rules will apply:

- Statements made in the course of the hearings will not be admissible at trial.
- The jurist, physician, and lawyer serving on the mediation panel will be ineligible to act as judge, witness, counsel, or otherwise thereafter in the case.

First Such Plan in Country

According to Justice Stevens, this is the first plan in the country to combine the personnel and talents of the judiciary with those of the legal and medical professions in such mediation procedures.

The panels will preside over a new special part of the court, he said, and the names of the panels and the calendars of cases assigned to them will be published in the *New York Law Journal* along with other court calendars and assignments.

He noted that the plan revolved from a public conference sponsored last year by the Interprofessional Committee of Doctors and Lawyers and from subsequent studies and conferences conducted by the court and the committee.

The medical representatives are appointed on recommendation of the New York County Medical Society. Present physician members are Dr. Carl Goldmark, Jr., vice-chairman, and Drs. Edgar P. Berry, W. Graham Knox, Stephen Norrlund, and George W. Slaughter.

Justice Stevens' statement said that appointment of the nonjudicial panels, to be designated as special mediators, "is expected to be from medical specialists in various branches of medicine upon recommendation of the medical society and of lawyers chosen mainly because of broad trial experience."

Normal Cells Made Malignant by Virus

Medical Tribune Report

SAN DIEGO, CALIF.—Two Salk Institute scientists, Walter Eckhart, Ph.D., and Dr. Renato Dulbecco, and a third from Princeton University, Max M. Burger, Ph.D., have reported that a virus can change the surface characteristics of a cell in such a way as to make it malignant.

Their experiments have used two small DNA viruses, polyoma and SV40. Earlier work by Dr. Dulbecco showed that viruses can change cells from normal to malignant and that viral genes persist in the malignant cells.

Last December, Dr. Dulbecco and Dr. Eckhart reported that these virus-induced changes can persist through succeeding generations of cells and that the changes depend on the function of a viral gene in the malignant cells.

Now, the Eckhart-Dulbecco-Burger team has shown, using polyoma virus, that the changes are to the surface of the cell, keeping it in a state that prevents it from receiving signals from the environment that normally would stop it from reproducing itself.

NEWS INDEX

Pediatrics (1, 3, 20, 22)

Prophylactic red cell transfusions may help sickle-cell children 1
Reimplantation of the carotid is advised in children with blocked arteries 3

Venereal Disease

Much work needed before syphilis vaccine can be applied to human subjects 1

Pollution

Today's detoxication system may yield clues for combating pollution effects 1

CLINICAL NEWS NOTE: "The treatment of deep burns and other types of graft suggest that skin from uremic donors provokes a less vigorous immune rejection response than normal skin. This may be due to antigen masking by substances produced in uremia." (Drs. H. Pierer and H. Fladerer; see page 3.)

Surgery

Skin from uremic donors preferred in treatment of deep burns 3

Legal Medicine (3, 29)

Mediation panel will hear medical malpractice suits filed in New York 3

Dermatology

Antimicrobial agents are believed to be present in human skin 6

Psychiatry

Functional improvement reported in families admitted to a psychiatric unit 10

Ob/Gyn (22, 24)

Sexual pleasure seen to increase in less than half of women on "the pill" 22

Virology

Investigator urges empiric approach to proving viral cause of cancer 27

FEATURE INDEX

Epigrams 1
Chess Problem to Consultation 1
Editorials 1
Letters to Tribune 15, 2
Sports Report 2
Economic Analysis 3
Medical Meeting Schedule 3
Immigration Medicine 31

Coming next issue see page 3

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Anxiety—frequent cause of gastrointestinal complaints or concomitant of gastrointestinal symptoms. Gastrointestinal complaints may be signals of functional gastrointestinal disorder or of organic gastrointestinal disease. In either case, severe anxiety frequently plays a prominent role in causing functional complaints or in complicating organic disease. Whenever excessive anxiety is a significant component of the clinical profile, adjunctive use of Librium® (chlordiazepoxide HCl) may be of value.

his gastrointestinal complaints are as real as

The normal duodenal bulb is approximately oval and exhibits a smooth triangular shape. This patient complains of bloating, sour stomach and nausea. He thinks he may have an ulcer, but thorough examination and x-rays show no sign of organic disease.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations

requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in woman of childbearing age requires that its potential benefits be weighed against

its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended; if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenoth-

azines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has

Librium (chlordiazepoxide HCl) is used concomitantly with certain specific types of other classes of drugs, such as anticholinergics, antacids and mucosal coating agents, whenever excessive anxiety contributes to gastrointestinal complaints or symptoms.

The duodenal bulb shows evidence of spasm and constriction at its waist, with a one-centimeter ulcer projecting superiorly from its base.

This patient complains of the same symptoms—bloating, sour stomach and nausea. He thinks he may have an ulcer, and thorough examination plus x-rays justify his high level of anxiety.

not been established clinically. **Adverse Reactions:** Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally

controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy. **Supplied:** Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl.

ROCHE Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

For relief of moderate to severe anxiety associated with gastrointestinal complaints and symptoms adjunctive

Librium 10 mg
(chlordiazepoxide HCl)

1 or 2 capsules
t.i.d./q.i.d.

Claim Antimicrobe Substance To Be Present in Human Skin

Medical Tribune Report

BOSTON—Indirect evidence for the presence of antimicrobial substances in human skin was presented here to the Society for Investigative Dermatology by Reza Aly, Ph.D., and his co-workers from the University of California School of Medicine in San Francisco.

Citing reports by other investigators that such substances exist in the lipid fraction of skin secretions and have been shown to rapidly kill a variety of microorganisms in vitro, Dr. Aly suggested that "if such agents are present on the skin surface, their removal should allow increased multiplication of applied organisms."

He and his co-workers found that, when one forearm was wiped with lipid solvents prior to application of the microorganisms, the destruction of *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Candida albicans* was significantly reduced to comparison to the destruction of the same microorganisms on a control forearm.

Healthy white male adult prison volunteers, who had not washed with germicidal soaps for seven days prior to the experi-

ment, were used as subjects. One forearm of each was washed for five minutes with acetone and the other forearm used as a control. The organisms were placed on the skin and covered immediately with plastic protective cups to prevent drying. After five hours, the organisms were harvested by a modified Petman-Burrows method.

Test Results Cited

Dr. Aly cited the following results:

- When *Staph. aureus* was applied (20 subjects), acetone-washed forearms had two- to 510-fold more organisms than the controls at five hours. A marked decrease in count from the original was seen in the controls, while the incubation period allowed persistence but not multiplication of the test organisms on the acetone-washed area.

- With *Str. pyogenes* (10 subjects), a decrease in overage count was noted in both forearms, with the reduction greater in the controls. A two- to 510-fold greater count was obtained in the acetone-washed area.

"Besides the obvious difference in counts between the two forearms, this ex-

NIH Trains Its Employees



Courses in lab animal care, glass blowing, administration, and other subjects are sponsored throughout the year by the Division of Research Services to further train National Institutes of Health employees. Right, Anita Blaser checks quality control samples of tissue culture media. Left, Frank Kling uses his method of dispensing thermolabile bacteriologic media. Both completed the D.R.S. basic chemistry class.

periment also illustrated the decreased ability of *Str. pyogenes* to survive on human skin as compared to *Staph. aureus* and *C. albicans*, Dr. Aly noted.

● *C. albicans* (10 subjects) was found to thrive better than either *Str. pyogenes* and *Staph. aureus* persistence, as did the fore-

control arms, with two- to 200-fold more on the acetone.

● No significant differences between washed and control arms were noted with *Pseudomonas aeruginosa* and *Escherichia coli*.

Dr. Aly said two additional experiments showed that the forced did not inhibit *Staph. aureus* persistence, as did the forearm, and the lipid solvent effect was demonstrable two hours after the organisms were applied but not at five hours. He said that "we do not interpret this data as disproof of the already demonstrated role of desiccation. We realize that drying is one of the most important factors in the disappearance of many bacteria, especially gram-negative rods. However, we do suggest a re-examination of the role of skin lipids or other antimicrobial substances in human skin."

Cosponsors were Drs. Howard I. Mahbach, Henry R. Shenefield, and Walter G. Strauss.

Cardiologists Begin Survey of Manpower

Medical Tribune Report

BETHESDA, MD.—A 15-month study of what the United States has and needs in professional manpower for cardiovascular diseases has been launched under the auspices of the American College of Cardiology, serving as administrator for a \$126,655 National Heart and Lung Institute contract. The study, to include questionnaires to several thousand practicing cardiologists, will be conducted by a team of investigators in medical education at the University of Southern California, who will work under a national advisory committee.

Stephen Abrahamson, Ph.D., Professor of Education at U.S.C., will be project director, and Dr. Forrest H. Adams, president of the American College of Cardiology, will be principal investigator and chairman of the advisory committee.

The study will yield data that will give a first-time look at present and future needs for manpower serving "the greatest and most important health problem in the United States as well as in many parts of the world," Dr. Adams said.

1962 was a bad year for Staph infection

In a hospital study from 1960 to 1967, only 2 positive staphylococcal lesions were noted among 34,262 infants washed with pHisoHex®. Both occurred in 1962.

In 5 additional studies,* of 1874 infants washed with pHisoHex®, Staph colonization was only 2.4%; while in 1160 "unwashed" control infants, colonization amounted to 45%.

Anti-Staph protection for the infant usually begins with a pHisoHex bath before he leaves the delivery room. It can be continued and strengthened throughout the infant's stay in the hospital nursery by bathing him daily with pHisoHex and having everyone who handles the infant wash his hands with pHisoHex before and after handling the baby. This routine builds a cumulative, rinse-resistant film of antibacterial hexachlorophene on the skin to form a powerful barrier against Staph and many other bacteria.

Mothers can maintain this antibacterial protection at home by bathing baby exclusively with pHisoHex. And nonalkaline, hypoallergenic pHisoHex is kind to skin. Won't dry or tend to irritate even when used frequently.

References: 1. Gluck, Louis; *Hosp. Practice* 3:38, Jan., 1968 (author's correction). 2. Payne, Margaret C.; Wood, H. F.; Korotkova, Walter, and Gluck, Louis; *Am. J. Epidemiol.* 82:305, Nov., 1965. 3. Gluck, Louis, and Wood, H. F.; *New England J. Med.* 265:1177, Dec. 14, 1961. 4. Simon, H. J.; Allwood-Paradee, Juan, and Treloar, Antonio; *Pediatrics* 38:294, Feb., 1966. 5. Gluck, Louis, and Wood, H. F.; *New England J. Med.* 268:1295, June 8, 1968. 6. Simon, H. J.; Yelks, S. J., and Gluck, Louis; *New England J. Med.* 265:1171, Dec. 14, 1961.

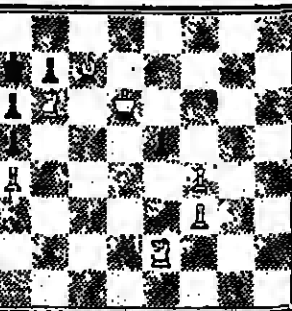
Winthrop Laboratories, New York, N.Y. 10016



pHisoHex
antibacterial skin cleanser
with 3% hexachlorophene

Chess Problem

Black



White

White to play and mate with fourth move. See page 20.

Esimil®
guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Indications
Hypertension (other than labile form) which cannot be adequately controlled with simpler agents; moderate to severe hypertension sustained hypertension, almost all forms of fixed and progressive hypertensive disease, when side effects of other antihypertensives prevent effective treatment.

Contraindications
Guinea pig: Proven or suspected pheochromocytoma; hypersensitivity to guanethidine. Do not use with MAO inhibitors. Hydrochlorothiazide: Anuria; discontinue drug if renal shutdown occurs for any reason. Progressive hepatic disease may accelerate development of hepatic coma. Do not give to patients with known allergy to thiazides or other sulfonamide-derived drugs.

Warnings
Guanethidine and hydrochlorothiazide are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with both drugs and their combination before prescribing, and patients should be warned not to deviate from instructions.

Guanethidine: Warn patients about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during initial dosage adjustment and with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking guanethidine.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage.

It is possible, without therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage.

Use in Pregnancy
The safety of guanethidine for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

Hydrochlorothiazide: Thiazides should be used with caution in pregnant or lactating patients

since this drug crosses the placental barrier and appears in breast milk and may cause fetal or neonatal hyperbilirubinemia, thrombocytopenia, or altered carbohydrate metabolism. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

Precautions
Guanethidine: Give cautiously to patients with severe coronary insufficiency, recent myocardial infarction, or cerebrovascular insufficiency. Give Esimil with extreme caution to those with severe cardiac failure.

Appetite suppressants (e.g., amphetamines), mild stimulants (e.g., ephedrine, methylphenidate), and tricyclic antidepressants (e.g., imipramine, propylthiouracil, doxepin) may decrease the hypotensive effect of guanethidine. Wait one week after discontinuing MAO inhibitors before starting guanethidine.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver function tests are advised during prolonged therapy.

Hydrochlorothiazide: Perform serum potassium, albumin, uric acid, and blood sugar tests prior to, and at appropriate intervals during therapy.

Watch patients for clinical signs of fluid or electrolyte imbalance (hypokalemia, hypochloremia, hyponatremia, hypocalcemia). Warning signs: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, dizziness, tachycardia, GI disturbances. Serum and urine electrolyte determinations may occur and may be indicated when patient is vomiting excessively or receiving parenteral fluids, steroids, or ACTH during brisk diuresis in presence of severe circulatory.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digoxin may cause metabolic effects of hypokalemia. Signs of digoxin intoxication may be produced by formulary doses of thiazides. In those with hepatic or renal disease, a low salt syndrome may complicate therapy.

Hyperuricemia (or frank gout) may be precipitated in certain patients. Insulin requirements in

diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide therapy. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

Adverse Reactions
Guanethidine: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions—fatigue, heart failure, less frequently—dyspnea, lightheadedness, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, loss of the lily, blurring of vision, parietal tenderness, myalgia, muscle tremor, mental depression, chest pain, tingling, chest parasthesias, nasal congestion, weight gain, and asthma in susceptible individuals.

Hydrochlorothiazide: Gastrointestinal—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (cholestatic hepatitis), pancreatitis, hyperglycemia, glycosuria. Central nervous system—dizziness, vertigo, parosmia, headache, xanthopsia. Dermatologic—hypersensitivity—purpura, photosensitivity, rash, urticaria, necrotizing angitis. Hematologic—leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Miscellaneous—muscle spasm, weakness, restlessness. When severe adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

Dosage
Optimal dosage must be determined for each individual. Adult: 10 mg guanethidine monosulfate present in Esimil is equivalent to 8.4 mg guanethidine sulfate USP (Tensilon®).

New Supplies
Tablets (white, scored), each containing 10 mg guanethidine monosulfate and 25 mg hydrochlorothiazide bottles of 100.

Before starting therapy, consult complete product literature.

CGA Pharmaceutical Company
Summit, New Jersey

all in the same boat many hypertensives do better on Esimil®

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Esimil may get things moving for all sorts of patients with moderate to severe hypertension. Often controls blood pressure when other antihypertensives fail. Usually keeps it controlled, too.

The key is guanethidine—perhaps the most effective antihypertensive available.

And with Esimil, dosages of both components—guanethidine and hydrochlorothiazide—are lower than with either used alone. So adverse reactions are usually minimized. Esimil. A smoother course for all sorts of hypertensives.



C I B A



One to two hours before surgery, 10 mg Injectable Valium (diazepam) I.M.



surroundings and disturbing procedures. Perhaps best of all, Injectable

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in: relief of skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; tetanus; status epilepticus and severe recurrent seizures; anxiety

prior to gastroscopy, esophagoscopy, and surgical procedures; cardioversion (I.V.).

Contraindications: In infants; in patients with known hypersensitivity to the drug; in acute narrow angle glaucoma; may be used in patients with open angle glaucoma receiving appropriate therapy.

Warnings: Inject I.V. slowly, directly into vein; take at least one minute for each 5 mg (1 ml) given. Do not mix or dilute with other solutions or drugs. Do not add to I.V. fluids. Rare reports of apnea or cardiac arrest noted, usually following I.V. administration, especially in elderly or very ill and those with limited pulmonary reserve; duration is brief; resuscitative facilities should be

available. Not recommended as sole treatment for psychotic or severely depressed patients. Should not be administered to patients in shock, coma, acute alcoholic intoxication with depression of vital signs. Caution against hazardous occupations requiring complete mental alertness. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy,



can promptly calm, lessening anxiety and tension associated with strange



Premedication for surgery

Injectable Valium (diazepam) is a useful premedicant for reducing undue anxiety. Recall of preoperative procedures is markedly diminished. When given in conjunction with narcotics, a reduction of narcotic dosage should be considered. (See summary of prescribing information.) Injectable Valium should not be mixed with other drugs, solutions, or fluids. The new 10-mg disposable syringe can help you observe this precaution at the same time it helps assure aseptic handling. Injectable Valium seldom significantly alters vital signs. Nevertheless, there have been infrequent reports of hypotension and rare reports of apnea and cardiac arrest, usually following I.V. administration. Resuscitative facilities should be available.

To relieve excessive preoperative anxiety, remember Injectable Valium (5 mg/ml) 2-ml ampul, 10-ml vial, 2-ml disposable syringe.

Valium (diazepam) markedly diminishes recall of the preoperative procedure.

lactation or women of childbearing age, weigh potential benefit against possible hazard to mother and child.

Precautions: If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium, such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Not recommended for bronchoscopy, laryngoscopy, obstetrical use, or in diagnostic procedures other than

gastroscopy and esophagoscopy. Laryngospasm and increased cough reflex are possible during gastroscopy; necessary countermeasures should be available. Hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Since effect with narcotics may be additive, appropriate reduction in narcotic dosage is possible. Use lower doses (2 to 5 mg) for elderly and debilitated. Safety and efficacy in children under 12 not established.

Side Effects: Drowsiness, fatigue, ataxia, confusion, depression, constipation, dysarthria, diplopia, headache, hypoactivity, hiccups, hypotension, incontinence, jaundice, nausea, changes

in libido, changes in salivation, phlebitis at injection site, urinary retention, skin rash, syncope, slurred speech, urticaria, tremor, vertigo, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbance and stimulation have been reported; should these occur, use of the drug should be discontinued. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy. Minor EEG changes, usually low-voltage fast activity, of no known significance.

ROCHE Roche Laboratories Division of Hoffmann-La Roche Inc. Nutley, N.J. 07110

Injectable Valium® (diazepam)

benefits every step of the way.

The Consultant

DR. DONALD A. Goss

Professor and Chairman, Department of Obstetrics and Gynecology,
Vanderbilt University School of Medicine, Nashville, Tenn.

What's new and important in infertility research?

There are several exciting areas in basic research in infertility which will soon be applied clinically. Primary among these is the research into the function of the prostaglandins. Another research area is the identification of steroid hormone receptor sites within sensitive tissues. These studies may well lead to a better understanding not only of problems related to infertility and steroid end-organ dysfunction but also provide a more physiologic means of contraception.

In clinical infertility the availability of clomiphene citrate and human chorionic gonadotropin for ovulation induction has received widespread utilization and provided the opportunity for childbearing to many families heretofore infertile. The surgical research done by Dr. Mulligan and his co-workers in tuboplasticity and the development of other surgical procedures related to infertility represents a great advance.



Dr. Goss

Amniocentesis and amniogram do carry a slight risk in normal pregnancy, but the procedure is relatively safe when done under image intensifier and using small amounts of dye.

There are varying reports concerning the incidence of congenital abnormalities in offspring of women over the age of 40, varying from 5 to 10 per cent. Of this group, mongolism represents the most common congenital abnormality that will carry to term. It must be emphasized that most individuals carrying a fetus with abnormal chromosomes will abort; therefore the absolute incidence is somewhat obscured by this factor. Maternal age, however, does appear to be significantly associated with the higher incidence of chromosome abnormalities. The importance of amniocentesis and karyotyping cannot be overemphasized. Most major medical centers today can provide this service and identify the fetus with grossly abnormal chromosomes.

What are the signs of choriocarcinoma? Should aspiration of amniotic fluid be carried out for diagnostic confirmation if trophoblastic disease is suspected during pregnancy?

There are several factors that are significant in establishing the diagnosis of choriocarcinoma. Every physician should be suspicious of the diagnosis of trophoblastic disease especially in patients who have a persistent watery discharge associated with intermittent bleeding. Malignant trophoblastic disease may occur as a primary tumor of ovarian structures or may be seen following fertilization—i.e., after miscarriage, delivery, or benign mole. When the diagnosis is suspected, amniogram with a water-soluble contrast medium is very helpful.

Amniocentesis and amniogram do carry a slight risk in normal pregnancy, but the procedure is relatively safe when done under image intensifier and using small amounts of dye.

Ultrasound offers an excellent diagnostic method for differentiation between normal pregnancy and trophoblastic disease. These techniques, now unfortunately available only in large medical centers, undoubtedly will be available throughout the country in a few years. Although the analysis of human chorionic gonadotropin titers is occasionally useful in the diagnosis, it must be remembered that in most instances the patient with trophoblastic disease will have HCG titers within the range seen in normal pregnancy.

The use of HCG titers is especially important in following the patient once diagnosis has been established. Following a negative result in a routine pregnancy test it is important that the patient be followed with radioimmunoassay for human chorionic gonadotropin for at least one year before conception be allowed. It is unfortunate that even today most of our patients referred with trophoblastic disease are not identified before the process has become metastatic. With adequate chemotherapy,

however, a significant majority of these patients are completely cured without removal of their pelvic organs.

Is hypertension, if adequately controlled, a contraindication to pregnancy? What antihypertensive regimen do you prefer, and what drugs should be avoided?

This is a very difficult question, because much depends upon the etiology of the patient's hypertension and whether or not the hypertension pre-existed before pregnancy occurred. If the hypertension can be controlled before conception and a positive diagnosis as to etiology established, the patient can maintain an uncomplicated pregnancy to term under adequate supervision. It is important, however, to eliminate those patients with renal disease, renal artery stenosis, etc., which might be cared for in a manner other than medical management of their hypertension.

Consultation with an internist is especially important. Careful attention to dietary sodium intake and use of diuretics may be necessary. One cannot specify specific antihypertensive regimen for all pregnant patients because the drugs utilized depend upon the etiology of the patient's hypertension. Hypertension appearing during pregnancy, especially the third trimester, is easily managed in most instances with diuretics, careful attention to sodium intake, and rest.

One drug which we feel should be avoided in pregnancy because of its rapid action and effect on electrolyte metabolism is furosemide. During the past year we have had one maternal mortality associated with the use of this drug and several patients become rapidly depleted in electrolytes. Therefore we prefer slower acting antihypertensive and diuretic agents.

Next Tribune Consultant



DR. SAMUEL J. FOMON, Professor of Pediatrics, University of Iowa Hospitals, Iowa City.

...and some questions he will answer:

- What is your attitude toward breast feeding?
- Which infant feeding practices are likely to have later consequences?
- Should formula-fed infants receive iron-fortified formulas?

Is it true that increased frequency of intercourse favors conception of males?

A great deal of research has been conducted in animals concerning the frequency and timing of intercourse in relation to the male/female ratio. At present there is very little statistical data available in humans. If frequent intercourse were to favor a male conceptus, however, we would certainly expect to find a higher percentage of males among first- and second-born babies, for the frequency of intercourse is usually greater in the first years of marriage. Studies in humans have usually been extrapolated from animal data and are not yet statistically significant.

Whole-Family Psychiatric Therapy May Result in Substantial Benefit

Medical Tribune World Service

HALIFAX, N.S.—Admission of entire families to the psychiatric unit of a Canadian general hospital resulted in functional improvement in most families, no matter which member was the object of primary care.

The Canadian Psychiatric Association was told here that in a four-year study, objections by both patients and hospital staff were fewer than expected and that the staff considered there was a moderate to high degree of benefit to 80 per cent of the families treated.

"But the lady at the admitting desk must be gently coaxed through her shock when it is suggested that she assign a male and a female to the same room," Dr. George

Molnar, chief resident in psychiatry at the clinical teaching unit of McMaster University, Hamilton, Ont., told the association's annual meeting here.

Dr. Molnar was coauthor of the study with Dr. Norman F. White, Assistant Professor of Psychiatry at the university.

The rationale for family admissions, Dr. Molnar said, was that admission of only the patient alone too often interfered with both assessment and treatment. With familiar family surroundings lacking, the patient did not behave in the way he did when his psychiatric problem originally arose.

Inferences Called Speculative

"Conclusions about the meaning of behavior, and about its origins, were based on observations in a false environment or on psychohistorical data collected through a screen of defenses and extraneous events," Dr. Molnar said. "Our inferences about interpersonal relations in the patient's native habitat were more speculative than informed."

Group, family, and individual therapy techniques were used in the study, with the family groups included with inpatients, day patients, and outpatients, Dr. Molnar said. Most common problems that required hospitalization of one family member were difficulty in child caring, general inability to function, risk of self-destruction, and marital breakdown. Seventeen of the mothers in the study suffered from postpartum disorders, with disorganized psychotic behavior and/or inability to care for their babies.

Both patients and staff at the hospital generally welcomed the presence of family units as a welcome change from the polished dreariness of hospital life, Dr. Molnar said. In families where the father was not the labeled patient, he often went to work as usual during the day, using the hospital as a home base.

Of 15 families that responded to an opinion poll up to three years after discharge, all but two thought the experience had resulted in improved family function. Most noted, however, that they had some difficulty in maintaining the situation in

From laboratory to laboratory.

Dalmane (flurazepam HCl) 30 mg usually induced sleep within 22 minutes, decreased nocturnal awakenings and provided 7 to 8 hours of sleep without need to increase dosage during the night, as demonstrated by more than 4300 hours of electro-oculographic measurements in five sleep laboratories.

From patient to patient.

Dalmane 30 mg was found to be effective for patients with difficulty in falling asleep, staying asleep or both.

From night to night.

Of three hypnotic agents—chloral hydrate 1000 mg, glutethimide 500 mg, and Dalmane 30 mg—evaluated in studies in a sleep laboratory, only Dalmane 30 mg both induced and maintained sleep for 14 consecutive nights of use.

With relative safety, as reported in clinical studies.

Instances of morning "hang-over" have been relatively infrequent; paradoxical reactions (excitement) and hypotension have been rare. Dizziness, drowsiness, light-headedness and the like were the side effects noted most frequently, particularly in the elderly or debilitated.

References: 1. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley, N. J. 2. Kales, A., et al. Arch. Gen. Psychiat. 23:226, 1970.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening, in patients with accompanying uncertainty of sleep patterns, and in adults of chronic "medical" sleep problems requiring restful sleep. Since amnestic effects are transient and infrequent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. First trimester should be avoided in patients under 15 years of age. Physical and psychological dependence have not been reported in long-term studies; however, in administration to a 33-hour-prison inmate, there was some evidence of dependence.

Precautions: In elderly and debilitated, and in dosage should be limited to 15 mg. In patients with chronic renal or hepatic disease, or in patients with other drugs having hypnotic or CNS depressant effects, consider potential additive effects. Exercise caution in patients with depression, anxiety, or with recent depression or suicidal tendencies. Proceed with caution in liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, light-headedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe reactions, including hypotension and coma, probably indicative of drug intoxication or overdose, have been reported. Also reported were headache, numbness, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, fatigue, weakness, apprehension, irritability, weakness, palpitations, chest pain, body and joint pains and GU complaints. There have also been rare reports of rash, hives, difficulty in swallowing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, and loss of appetite, depression, slurred speech, confusion, restlessness, hallucinations and elevated SGOT, SGPT, total and direct bilirubin and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

Dalmane®

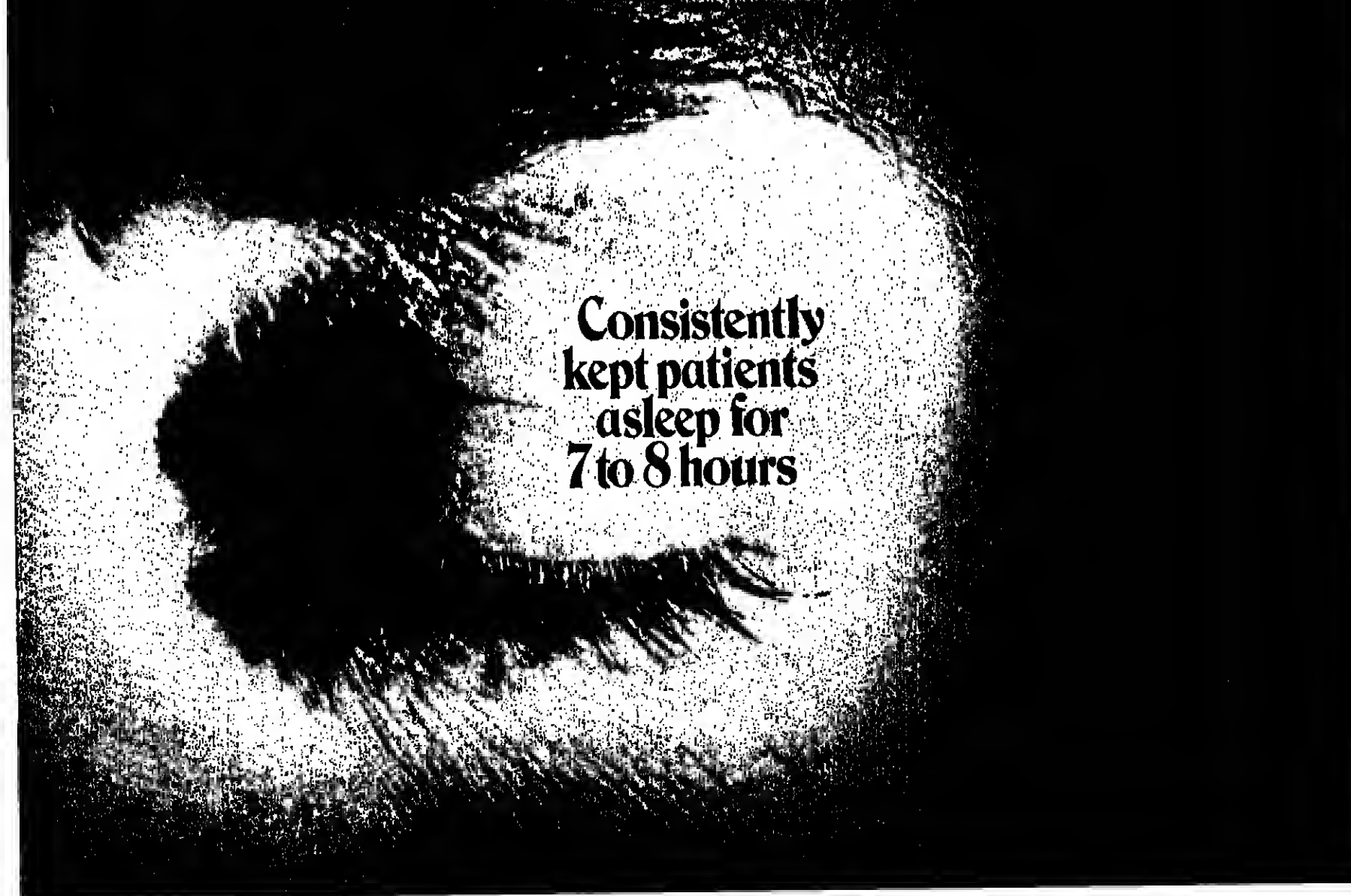
(flurazepam HCl)

One 30-mg capsule h.s.—usual adult dosage.

One 15-mg capsule h.s.—initial dosage for elderly or debilitated patients.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110



Consistently
kept patients
asleep for
7 to 8 hours

the unoonstipators

Medical management of constipation need not resort to irritants, bulky, laxative emollients, dehydrating salines, or contact irritants. A sensible method is to prescribe

SENOKOT Tablets/Granules—a standardized vegetable derivative with a virtually colon-specific laxative action that is both gentle and predictable. Acting not through irritation of gastrointestinal mucosa, but through gentle stimulation

of the Auerbach's plexus, SENOKOT Tablets/Granules represent a physiologic approach to the alleviation of constipation.

The Purdue Frederick Company
Yonkers, N.Y. 10701

Senokot tablets/granules
(see directions on packaging)



When analgesia is needed for a long period

- Comparable to codeine in analgesic efficacy: one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine.
- Prolonged analgesia between doses: relieves pain usually for 3 hours or longer. Onset of significant analgesia usually occurs within 15 to 30 minutes.
- Tolerance to the analgesic effect of Talwin Tablets has not been observed and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- Infrequently causes decrease in blood pressure or tachycardia; rarely causes respiratory depression or urinary retention; seldom causes diarrhea or constipation.
- Generally well tolerated by most patients: if dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See Product Information following for full discussion of all adverse reactions and other prescribing information.)
- Not subject to narcotic controls: convenient to prescribe—day or night.

A time for Talwin[®] brand of pentazocine (as hydrochloride) 50mg. Tablets

عقار مسكن



See next page for brief summary of Prescribing Information.

moderate to severe pain

A time for Talwin

brand of

pentazocine 50mg. Tablets

(as hydrochloride)

Contraindications: Talwin should not be administered to patients who are hypersensitive to it. **Warnings:** Head Injury and Increased Intracranial Pressure. The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in doses by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain. **Acute CNS Manifestations.** Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: Certain Respiratory Conditions. Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accumulation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.



Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effects. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include gastrointestinal: nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. **CNS effects:** dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, ataxia, visual blurring and focusing difficulty, hallucinations (see **Acute CNS Manifestations** under **WARNINGS**); and rarely tremor, irritability, excitement, tinnitus. **Autonomic:** sweating; infrequently flushing; and rarely chills. **Allergic:** infrequently rash; and rarely urticaria. **Cardiovascular:** infrequently decrease in blood pressure, tachycardia. **Other:** rarely respiratory depression, urinary retention.

Dosage and Administration: Adults. The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin. **Children Under 12 Years of Age.** Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see **WARNINGS**). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: Manifestations. Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are not effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®; available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®), may be of value if respiratory depression occurs.

Talwin is not subject to narcotic control.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottle of 100.

Winthrop Winthrop Laboratories, New York, N.Y. 10016

Medical Tribune

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Good—and Outstanding

THE FOOD AND DRUG ADMINISTRATION is fortunate to be headed by a commissioner who is a physician and an administrator and who excels at both disciplines. Since taking command, Dr. Charles C. Edwards has had the herculean task of reorganizing and restructuring the FDA and of recruiting scientific and technical manpower for it. Along with this major chore, he has simultaneously had to confront sticky problems and make decisions in the area of public health while under fire from contending vested interests and while constantly reporting to Congressional committees. All this, in addition to the almost impossible task of the FDA's day-to-day regulatory activities.

Although MEDICAL TRIBUNE has often taken issue with FDA decisions, it has done so with admiring respect for Commissioner Edwards' achievements, his surgical coolness under stress, and his round-the-clock dedication to his responsibilities.

In a recent speech at the Symposium on National Policy and the Life Sciences, held at Woods Hole, Mass., Dr. Edwards emphasized that public interest and sophisticated in scientific matters must be encouraged by the scientific community, which must see to it that this interest "is predicated upon and nourished by scientific fact and not emotionalism." Dr. Edwards posed a number of fundamental questions that confront the FDA and that are of great importance to physicians, to patients, and to the public weal in general.

He asked: (1) "How do we get across to the public and to our public critics the double face of our responsibilities—the positive responsibility to regulate good

products onto the market as well as the negative responsibility to regulate bad products off the market?" (2) "Where do we draw the line in demanding scientific proof of safety and efficacy of existing products in order to be certain we are protecting the public and yet not stifling research to discover still more beneficial cures?" (3) "How do we deal with the constant problem of having to make regulatory decisions in the face of incomplete and inconclusive scientific knowledge?" (4) "Finally, in the face of doubt and skepticism, how do we in government, in the scientific community, and industry restore public confidence in our decision making?"

This last crucial question calls for understanding and participation on the part of the resident many of the worth-while advances in medicine he has not had the time to observe firsthand. The resident physician would learn from the resident many of the worth-while advances in medicine he has not had the time to observe firsthand. The resident physician would learn from the resident many of the worth-while advances in medicine he has not had the time to observe firsthand.

Dr. Edwards has been a good, indeed an outstanding, commissioner. If he successfully provides the answers to the questions he posed, he may well be a great one.

Saving Lives or Saving Lockheed

WHEN IT COMES to appropriating money in these difficult days, one is baffled by the order of our governmental priorities. Appropriations for research have been reduced, medical schools by the

score are at the brink of disaster, the physical plants of thousands of our hospitals are a disgrace.

What should take priority—saving Lockheed or saving lives?

VD

PROSPECTS for the availability of vaccines against syphilis and gonorrhea in the immediate future do not seem bright if judged by the latest news of a workshop session at the International Congress of

Immunology (see page 1). Meanwhile, the chances for stemming an ever-widening incidence of venereal disease in this country depends on reporting patients and thus helping ease finding.

Antimicrobial Substances in Skin?

CLINICAL QUOTE: "We interpret the data presented here as possible substantiation of the role of antimicrobial substances on skin in the destruction of certain pathogenic microorganisms. The disappearance of Staph. pyogenes and Staph. aureus in moist environments (with an occlusive device) suggests that these organisms are sensitive to the presence of antimicrobial substances

due to some chemical mechanisms. It was shown that when the forearm was wiped with acetone, the destruction of Staph. aureus, Staph. pyogenes, and C. albicans was significantly reduced." (Raza, Aiy, Ph.D., and Drs. H. I. Maibach, H. R. Shinefield, and W. G. Strauss, at the Society for Investigative Dermatology meeting in Boston; see page 6.)



"Wall it's finally happened, doctor—you're booked up for the rest of your life."

Rural Doctor Shortage

Editor, MEDICAL TRIBUNE:

Everyone admits that the doctor shortage in rural areas is acute, but no one—well, hardly anyone—seems to be doing anything practical about it. It seems to me the following plan is worth while, for various reasons.

Every resident physician should be required, as part of his training, to spend one month (or preferably six weeks) in at least one of his residency years with a rural practitioner.

The advantages are, I believe, evident: 1. The resident would learn the practical as well as scientific aspect of actual practice in office, home, or small community hospital, as compared with the ivory-tower atmosphere and methods of the medical center. He could learn to depend less on many expensive, time-consuming, and unnecessary procedures he has learned in the hospital.

2. The rural physician would learn from the resident many of the worth-while advances in medicine he has not had the time to observe firsthand.

3. The resident would be paid for his "locum tenens" or associate status in addition to his regular salary.

4. The rural physician would be freed to take time off for postgraduate study and/or vacation.

5. (and this may be the most important). The resident on loan would, there is good reason to hope, become sufficiently interested in rural practice and its many rewards to decide to settle in the same or similar rural community on finishing his training, as opposed to the present trend toward overspecialization and/or a life of often unrewarding research.

HAROLD J. HARRIS, M.D.
Westport, N.Y.

'Occupational Hazard'

Editor, MEDICAL TRIBUNE:

As a doctor's wife, I have become aware of an "occupational hazard" with which you may also be confronted. Unsolicited drugs are constantly sent to my husband through the mail by drug companies. These are left in our mailbox (on the street away from the house) or at his office. Anyone is able to pick up the package from our mailbox. We will know the problems and prevalence of drug addiction in our own areas, and there is no control over who gets these packages.

Most of these unsolicited drugs are never prescribed by my husband, which causes a problem of disposal. If we toss them in the wastebasket, they may be retrieved by our children or someone else. If we carefully unwrap each capsule and

flush it into the sewage system, we risk pollution of our waters.

There is a solution. As each package arrives, write on the front of it: "Refused. Return to sender." You need not add postage; it will be paid by the drug company. Then, write a simple note on your own stationery to that same return address: "I do not approve of sending drugs through the mail. Please remove my name from your mailing list. Drugs sent to me in the future will be returned unopened. Thank you."

Obviously, I feel that this is an important situation for doctors to consider. If you agree, please take a few minutes each month to help solve the problem. I have.

CONSTANCE EAY BURNS
Palos Verdes Peninsula, Calif.

'Last-Ditch Fight'

Editor, MEDICAL TRIBUNE:

The medical profession is now facing an absolute "last-ditch" fight against socialized medicine. It is obvious that immediate and drastic action must be taken. I am proposing such action, to which I have given much thought and have received much verbal support from many persons, not only physicians.

The great majority of our lawmakers in Washington are lawyers by profession and are well aware that when they retire or fail to be re-elected, they usually have a lucrative private law practice waiting for them. If they could be influenced to give some thought to their personal futures, I believe the great majority, regardless of political party, would quickly reconsider any further efforts toward socialized medicine.

Specifically, what I am proposing is an all-out "grass-roots" demand for socialized law.

The great majority of voters, sometime in their lives, have needed to employ the services of a good private attorney and found their fees rather high for services rendered. In fact, to the lower income brackets, with whom I've had close professional relations as a psychiatrist, truly good legal services are unobtainable due to high fees.

Personally, I am opposed to socialism in general, but I do believe that if the fear of socialized law could be dramatically presented to our lawmakers, we would not hear too much more about socialized medicine from them. Sometimes in our lives we must fight "fire with fire." At least it is worth some consideration thought and action in this fight against socialized medicine.

HARRY M. RICKETTS, Jr., M.D.
Dallas, Tex.



Two-year-old patient places blocks using prostheses under aid of occupational therapist Joanne Sesong. Dr. Ames observes. Right, physical therapist Carol Wildsmith helps triple amputee.



Early Prostheses Fittings Found to Ease Adaptation

CONGENITAL AMPUTEES, some as young as three months, are fitted with prostheses in a rehabilitative program at the Children's Hospital of Philadelphia. Working with very young patients facilitates adaptation to the limbs and lessens the chances of later rejection, stresses Dr. Mary Ames, pediatrician and coordinator of rehabilitative services. A result is that the staff must occasionally improvise. Thus skates were provided to one 14-month-old with artificial legs who could not handle crutches easily. The progress of each of the 18 participants is evaluated at a monthly meeting.

Prosthetist Ronald Parmelee measures one-year-old child for an artificial limb. Unlike previous limb, new one will have a control cable, as infant's muscles are developing.



Affair of the heart: Train and fire engine rides, "pond" fishing, and ring tossing delighted 65 former heart surgery patients, aged two to 14, and families at the first Medical University of South Carolina picnic-reunion. Dr. Arno R. Hohn, Professor of Pediatric Cardiology and director of the division, launched the idea for the event; the pediatrics personnel supplied the manpower. Left, Dr. Hohn with former patient. Above, one of several clowns at gathering tries to coax a smile from girl.

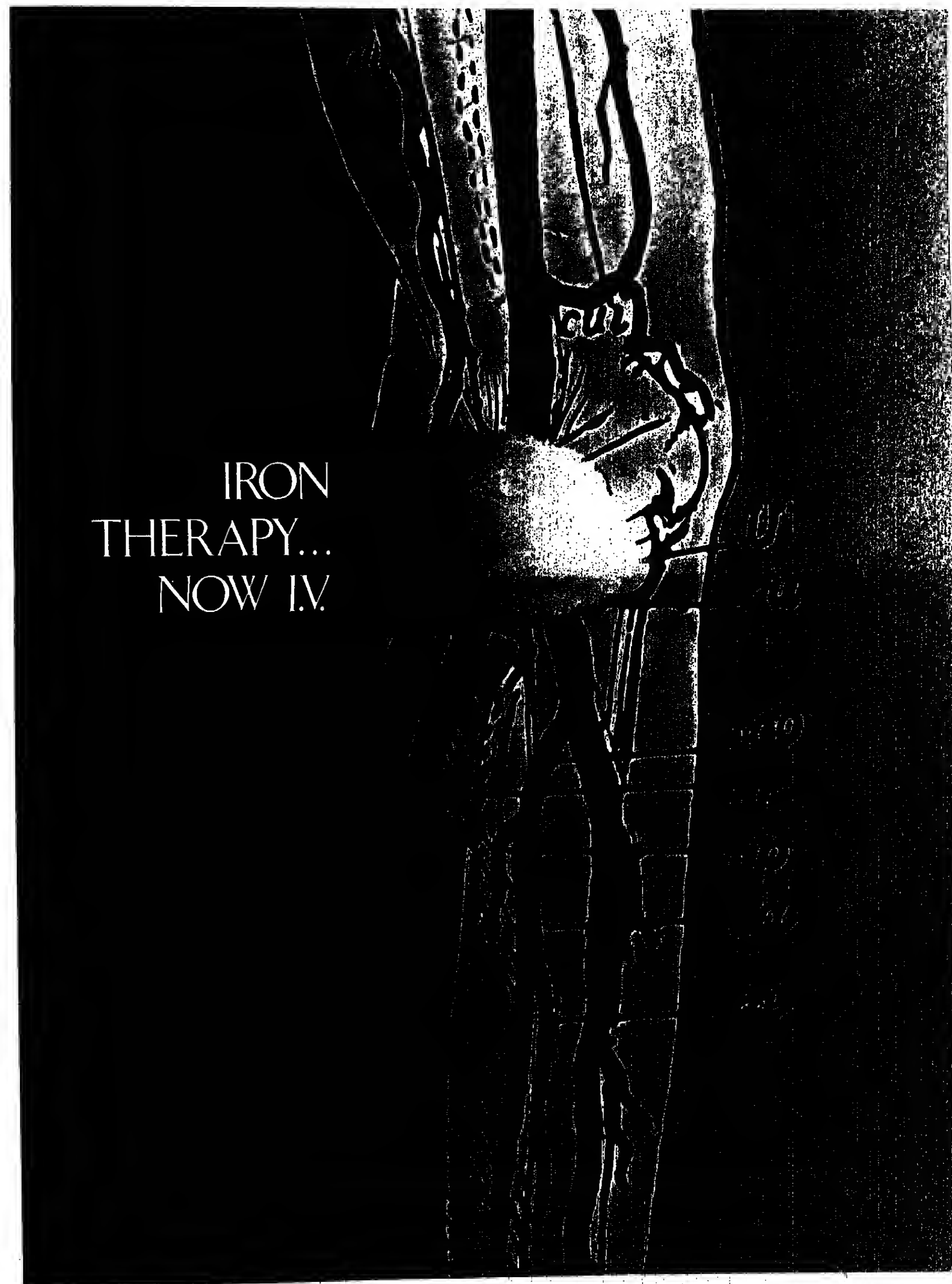


Missing limb
lab animals will be in
School of Medicine
Thomas Clarkson

Medical Tribune

Section II • Advertisement

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THERAPY...
NOW I.V.

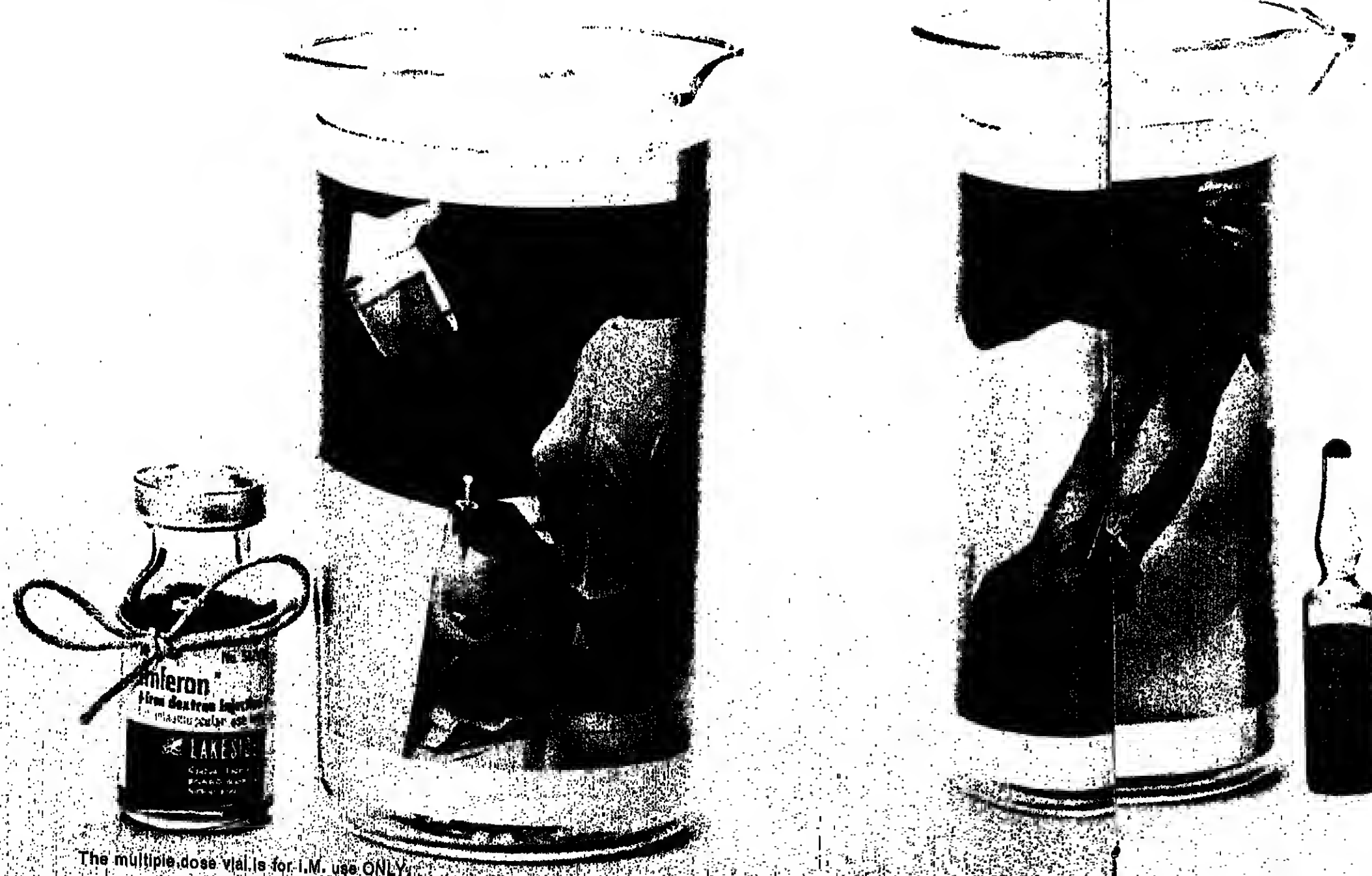


IMFERON[®] I.M./I.V. (iron dextran injection)

- predictably raises hemoglobin
- rapidly builds iron reserves
- bypasses the sensitive gastrointestinal tract

“The parenterally administered iron preparation of choice is iron dextran. It may be given intramuscularly or intravenously.”¹

1. Council on Foods and Nutrition: Iron Deficiency in the United States, JAMA 203:407-412 (Feb. 5) 1968.



The multiple dose vial is for I.M. use ONLY.

IMFERON IS USEFUL WHEN YOUR PATIENTS ARE RESISTANT TO, INTOLERANT OF, OR OTHERWISE UNRESPONSIVE TO ORAL IRON.

THERE'S A NUMBER OF REASONS FOR USING IMFERON:

For the treatment of iron deficiency anemia: intramuscular or intravenous injections of iron are advisable solely for use in those patients in whom iron deficiency anemia is present, its cause has been determined and, if possible, corrected, and in whom oral administration of iron is unsatisfactory or impossible; for example:

- intolerance to oral preparations;
- resistance to oral iron therapy;
- rapid replenishment of iron stores in selected patients in whom oral therapy is ineffective, such as
hypochromic anemia of infancy and
hypochromic anemia of the last trimester of pregnancy;
- selected hemorrhagic cases (appropriate steps should be taken to correct and prevent any excessive blood loss that may have been revealed as an etiologic factor);
- to replace postoperative transfusions to some degree;
- in those patients who cannot be relied upon to take oral medication.

IMFERON Injected Intramuscularly is the preferred and recommended route of administration. Intravenous use of IMFERON should be limited to the following circumstances:

- Insufficient muscle mass for deep Intramuscular Injection
- Impaired absorption from the muscle due to stasis or edema
- The possibility of uncontrolled intramuscular bleeding due to trauma as may occur in hemophilia
- Where massive and prolonged parenteral therapy is indicated as may be necessary in instances of chronic substantial blood loss, such as familial telangiectasia
- In those circumstances where, in the opinion of the physician, the benefit of intravenous administration substantially outweighs the risk.

See back page for complete prescribing information.

••With the advent of iron-dextran (Imferon) for intramuscular injection, parenteral administration of iron has become a safe, highly efficient procedure.***

some conditions
iron deficiency
anemia



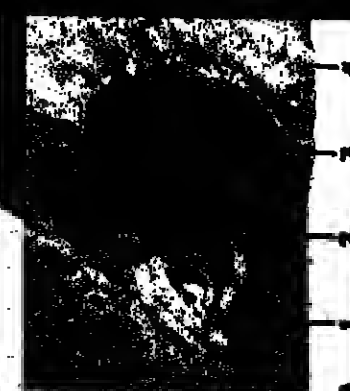
epistaxis



menorrhagia



multiple pregnancies



peptic ulcer



regional ileitis

IRON FROM VARIOUS SOURCES

Source	IRON ABSORBED (%)*	
	Normal	Iron deficient Adults
IMFERON® I.V.	up to 99	up to 99
Veal Muscle	20.2	27.1
Lettuce, Spinach	3	9
Liver	8	22
Hemoglobin (raw)	10	22
Hemoglobin (cooked)	7	12
Ferrous sulfate	8.2-12	20

*Based on relatively equal amounts of iron consumed.

2. Modell, W. J. Design for the Use of Drugs in Hematologic Disorders. *Drugs of Choice* 1970-71, pg. 590.

Typical case histories I.M./I.V. excellent clinical response

Age	Sex	Diagnosis	Hemoglobin before Imferon	Hemoglobin after Imferon	Route of administration
18	F	Cancer ¹	7.3 Gm./%*	10.5 Gm./%—4 weeks 11.2 Gm./%—9 weeks 13.4 Gm./%—12 weeks	I.M.
		Leukemia, myeloid ²	7.3 Gm./%*	10.5 Gm./%—4 weeks 11.2 Gm./%—9 weeks 13.4 Gm./%—12 weeks	I.M.
		Leukemia, myeloid ²	7.3 Gm./%*	10.5 Gm./%—4 weeks 11.2 Gm./%—9 weeks 13.4 Gm./%—12 weeks	I.M.
		Leukemia, myeloid ²	7.3 Gm./%*	10.5 Gm./%—4 weeks 11.2 Gm./%—9 weeks 13.4 Gm./%—12 weeks	I.V.
		Leukemia, myeloid ²	7.3 Gm./%*	10.5 Gm./%—4 weeks 11.2 Gm./%—9 weeks 13.4 Gm./%—12 weeks	I.V.
78		Leukemia, myeloid ²	4.5 Gm./%	8.3 Gm./%—4 weeks 10.3 Gm./%—7 weeks	I.V.
17	F	Postpartum bleeding, acute infectious mononucleosis ⁴	7.4 Gm./%	12.3 Gm./%—5 weeks	I.V.

* Using 14.0 Gm./% as base.

1. Balch, L. M., and Podman, D. A. *Lancet* 1962, 1054.
2. Grunberg, A., and Ellet, J. L. *Arch. Int. Med.* 1971, 105.
3. Hagdon, A. S. *Proc. Staff Meet. Mayo Clin.* 26/7/61, 1971.
4. Cecil, Department of Clinical Research, Laboratory, West, W. O. Lexington, Kentucky.

now Imferon for I.V. administration...with almost complete iron availability

IMFERON® I.M./I.V.
(iron dextran injection)

See back page for complete prescribing information.

AN IRON FOR ALL AGES

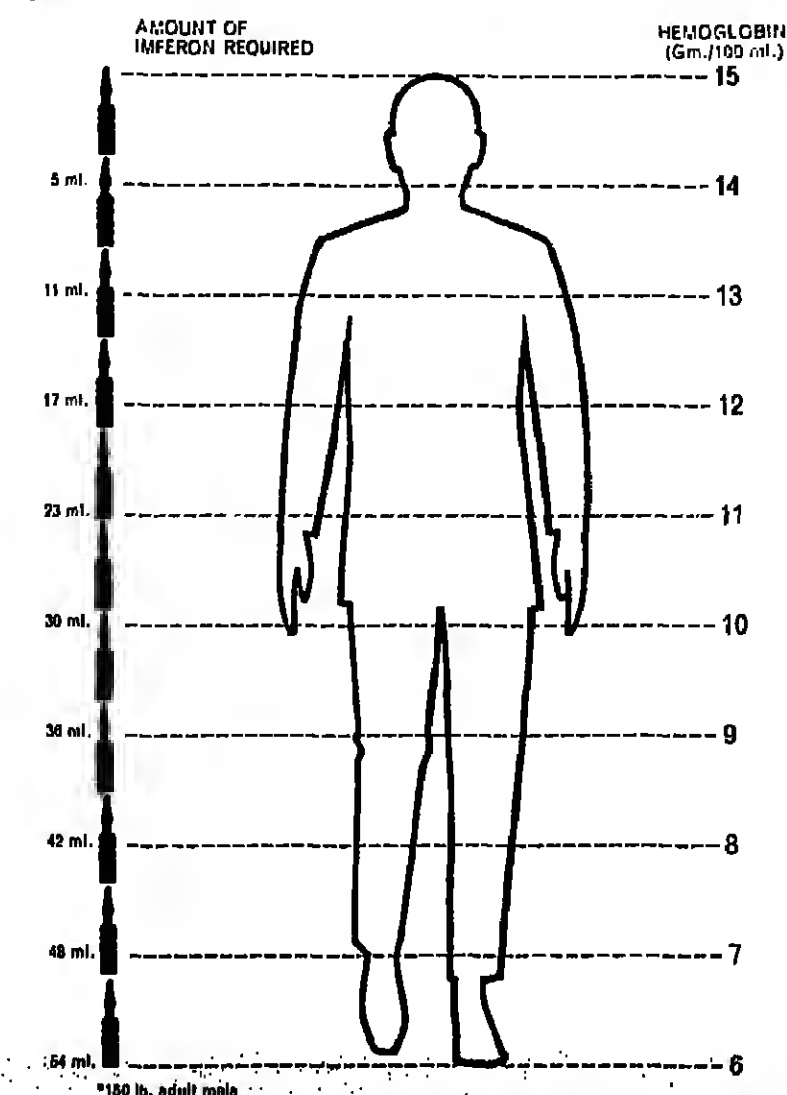
(a dosage for all sizes)

TABLE: TOTAL NUMBER OF ml. OF IMFERON (Iron dextran Injection) REQUIRED IN A COURSE OF TREATMENT

Patient's Weight in Pounds	Observed Hemoglobin				
	30% (4.4 Gm./ 100 ml.)	40% (5.9 Gm./ 100 ml.)	50% (7.4 Gm./ 100 ml.)	60% (8.9 Gm./ 100 ml.)	70% (10.4 Gm./ 100 ml.)
180	76 ml.	64 ml.	54 ml.	43 ml.	32 ml.
170	72	61	51	41	31
160	68	57	48	38	29
150	63	54	45	36	27
140	59	50	42	34	25
130	55	47	39	31	23
120	51	43	36	29	22
110	46	39	33	26	20
100	42	36	30	24	18
90	38	33	27	22	16
80	34	29	24	19	15
70	30	25	21	17	13
60	25	22	18	15	11
50	21	18	15	12	9
40	17	15	12	10	7
30	10	9	7	6	5
20	7	6	5	4	3
10	4 ml.	3 ml.	2 ml.	2 ml.	2 ml.

for example...

the amount of Imferon required to raise an average adult's* hemoglobin to 15 Gm./%, and replenish iron stores, would be as follows:



DOSAGE FOR INTRAMUSCULAR USE: The total amount of IMFERON (Iron dextran Injection) required is calculated from the formula or table (see preceding table). Inject a test dose of 0.5 ml. the first day. If no indications of adverse reactions are apparent, proceed to administer IMFERON according to the following schedule until the calculated total amount required has been reached. Each day's dose should ordinarily not exceed 0.5 ml. (25 mg. of iron) for infants under 10 lbs., 1.0 ml. (50 mg. of iron) for children under 20 lbs., 2.0 ml. (100 mg. of iron) for patients under 110 lbs., and 5 ml. (250 mg. of iron) for others. Inject only into the upper outer quadrant of the buttock—never into the arm or other exposed area. Inject deeply, with a two- or three-inch 18 or 20 gauge needle. If the patient is standing, he should be bearing his weight on the leg opposite the injection site, or if in

bed, he should be in the lateral position with injection site uppermost. To avoid injection or leakage into the subcutaneous tissue, a Z-track technique (displacement of the skin laterally prior to injection) is recommended.

DOSAGE FOR INTRAVENOUS USE: The total amount of IMFERON (Iron dextran Injection) required is calculated from the formula or table (see preceding table). This is given in a dose of 0.5 ml. the first day to test for and minimize the chance of toxic reactions. Within two or three days the dosage may be raised to 2 ml. per day, and given thus until the calculated total amount required has been reached. The IMFERON is given undiluted and slowly (one minute per ml. or fraction thereof).

NOTE:

The total cumulative amount required to restore hemoglobin and replenish iron stores may be approximated from the formula:

$0.3 \times \text{body weight in pounds} \times (100 - \text{patient's hemoglobin in gram percent}) \times 100$
= milligrams total iron to be injected.

(to calculate dose in ml. of Imferon, divide this result by 50)

now Imferon for IV administration... with almost complete iron availability

IMFERON® I.M./I.V.
(iron dextran injection)

See back page for complete prescribing information



IMFERON® I.M./IV. (iron dextran injection)

WARNING:

THE PARENTERAL USE OF COMPLEXES OF IRON AND CARBOHYDRATES HAS RESULTED IN FATAL ANAPHYLACTIC-TYPE REACTIONS. DEATHS ASSOCIATED WITH SUCH ADMINISTRATION HAVE BEEN REPORTED. THEREFORE, IMFERON SHOULD BE USED ONLY IN THOSE PATIENTS WHERE CLEARLY ESTABLISHED INDICATIONS EXIST, CONFIRMED BY APPROPRIATE LABORATORY INVESTIGATIONS CORROBORATING IRON DEFICIENCY ANEMIA NOT AMENABLE TO ORAL IRON THERAPY.

DESCRIPTION:

IMFERON® (iron dextran injection)—a dark brown, slightly viscous liquid complex of ferric hydroxide and dextran in a 0.05% sodium chloride solution for injection. It contains 50 mg. of elemental iron per ml.

ACTION:

The iron dextran complex is dissociated by the reticuloendothelial system, and the ferric iron is transported by transferrin and incorporated into hemoglobin.

INDICATIONS:

For the treatment of iron deficiency anemia: Intramuscular or intravenous injections of iron are advisable solely for use in those patients in whom iron deficiency anemia is present, its cause has been determined and, if possible, corrected, and in whom oral administration of iron is unsatisfactory or impossible; for example: intolerance to oral preparation; resistance to oral iron therapy; rapid replacement of iron stores in selected patients in whom oral therapy is ineffective, such as hypochromic anemia of infancy and hypochromic anemia of the last trimester of pregnancy; selected hemorrhagic states (appropriate steps should be taken to correct and prevent any excessive blood loss that may have been revealed as an etiologic factor); to replace post-operative transfusion to correct anemia in those patients who cannot be relied upon to take oral medication.

IMFERON (iron dextran injection) injected intramuscularly is the preferred and recommended route of administration. Intravenous use of IMFERON should be limited to the following circumstances:

- Insufficient muscle mass for deep intramuscular injection
- Impaired absorption from the muscle due to atelectasis or edema
- The possibility of uncontrolled intramuscular bleeding due to trauma or may occur in hemophilia
- Where massive and prolonged parenteral therapy is indicated or may be necessary in instances of chronic substantial blood loss, such as familial telangiectasia
- In those circumstances where, in the opinion of the physician, the benefit of intravenous administration substantially outweighs the risk.

CONTRAINDICATIONS:

Hypersensitivity to the product. All anemias other than iron deficiency anemia.

WARNINGS:

This preparation should be used with extreme care in the presence of serious impairment of liver function.

A risk of carcinogenesis may attend the intramuscular injection of iron-carbohydrate complexes. Such complexes have been found under experimental conditions to produce sarcomas when injected in rats, mice and rabbits, and possibly in hamsters, in very large doses. The number of tumors produced was relatively small, and such tumors have not been produced in guinea pigs. The long latent period between the injection of a potential carcinogen and the appearance of a tumor makes it impossible as yet to measure the risk in man. However, the risk of carcinogenesis in man, following recommended therapy, appears to be extremely small.

Usage in Pregnancy: In animals, fetal abnormalities have been demonstrated when IMFERON (iron dextran injection) was given early in pregnancy. Safe use of IMFERON (iron dextran injection) has not been established with respect to

adverse effects on human fetal development. IMFERON should not be used in early pregnancy and should be used in women of childbearing potential only when, in the judgment of the physician, the potential benefits outweigh the possible hazards.

PRECAUTIONS:

Unwarranted therapy with parenteral iron will cause excess storage of iron with the consequent possibility of exogenous hemosiderosis. Such iron overload is particularly apt to occur in patients with hemoglobinopathies and other refractory anemias which might be erroneously diagnosed as iron deficiency anemia.

Patients with iron deficiency anemia and rheumatoid arthritis may have an acute exacerbation of joint pain and swelling following the intravenous administration of IMFERON (iron dextran injection).

ADVERSE REACTIONS:

Anaphylactic reactions including fatal anaphylaxis; severe febrile reactions with chills and myalgia; variable degrees of soreness and inflammation at injection site (IM injection); brown skin discoloration at injection site (IM injection); local phlebitis at injection site (IV injection); peripheral vascular "flushing" with overly rapid IV administration; hypotensive reaction; possible arthritic reaction in patients with quiescent rheumatoid arthritis; minor reactions may include headache, transitory paresthesias, nausea, shivering, itching, and rash.

DOSEAGE AND ADMINISTRATION:

Periodic hematologic determinations are to be used as a guide in therapy, bearing in mind that iron stores may lag behind the appearance of normal blood morphology.

The following table provides a convenient method of determining the approximate quantity (in ml.) of IMFERON (iron dextran injection) needed for restoration of the hemoglobin and body stores of iron.

The requirements for individuals weighing 30 pounds or less have been reduced to 50% of the formula cited; such patients may be considered to be infants whose "normal hemoglobin" is between 6 months and 30 months of age is roughly 12 Gm., rather than the 14.5 Gm. on which the rest of the table is based.

DOSEAGE FOR INTRAMUSCULAR USE:

The total amount of IMFERON (iron dextran injection) required is calculated from the formula or table (see above). Inject a total dose of 0.5 ml. the first day. If no indications of adverse reactions are apparent, proceed to administer IMFERON according to the following schedule until the calculated total amount required has been reached. Each day's dose should ordinarily not exceed 0.5 ml. (25 mg. of iron) for infants under 10 lbs., 1.0 ml. (50 mg.) for children under 20 lbs., 2.0 ml. (100 mg. of iron) for patients under 110 lbs., and 5 ml. (250 mg. of iron) for others.

Inject only into the upper outer quadrant of the buttock—never into the arm or other exposed area. Insert needle with a two- or three- 16 or 18 gauge needle. In the event of a fainting, he should be bearing his weight on the legs. After the injection site, or if in bed, he should be in the supine position with injection site uppermost. To avoid infection, cleanse the skin with antiseptic solution. A Z-track technique of the skin (laterally prior to injection) is recommended.

TABLE: TOTAL NUMBER OF ml. OF IMFERON (iron dextran injection) REQUIRED IN A COURSE OF TREATMENT

Patient's Weight in (4.4 Gm.) Pounds	OBSERVED HEMOGLOBIN				
	30% 100 ml.	40% 100 ml.	50% 100 ml.	60% 100 ml.	70% 100 ml.
10	4 ml.	8 ml.	0 ml.	2 ml.	2 ml.
20	7	6	5	4	3
30	10	9	7	6	5
40	17	15	10	10	7
50	21	18	13	10	6
60	25	22	16	12	11
70	30	26	21	17	13
80	34	29	24	19	15
90	38	32	27	22	16
100	42	36	30	24	18
110	46	39	33	26	20
120	51	43	36	29	22
130	55	47	39	31	23
140	59	50	42	34	25
150	63	54	45	36	27
160	68	57	48	38	30
170	72	61	51	41	31
180	76	64	54	43	32

The total cumulative amount required to restore hemoglobin and replenish iron stores may be approximated from the formula:

$$0.3 \times \text{Body weight in pounds} \times \left(\frac{100 - \text{Patient's hemoglobin in gram percent} \times 100}{14.5} \right) = \text{Milligram total iron to be injected}$$

(To calculate dose in ml. of IMFERON, divide this result by 50)

DOSEAGE FOR INTRAVENOUS USE:

The total amount of IMFERON (iron dextran injection) required is calculated from the formula or table (see above). This is given in a dose of 0.5 ml. the first day to test for and minimize the chance of toxic reactions. Within two or three days the dosage may be raised to 0 ml. per day, and given thus until the calculated total amount required has been reached. The IMFERON is given undiluted, and slowly (one minute per ml. or fraction thereof).

SUPPLIED:

For intravenous or intramuscular use:
NOC 73-50-09 5 ml. ampule, boxes of 10.
NOC 73-51-34 5 ml. ampule, boxes of 4.

For intramuscular use ONLY:
NOC 73-52-22 10 ml. multiple dose vial containing phenol 0.4% as preservative, boxes of 5.

IMFERON® (iron dextran injection) is distributed by Lakeside Laboratories, Inc., under license from Faeon Pharmaceuticals.

LAKESIDE LABORATORIES, INC.
Milwaukee, Wisconsin 53201

now Imferon for IV administration with almost complete iron availability



the iron your patients can't forget to take

Gentlemen, I am interested in Imferon. Please send me

- ☐ Samples of Imferon
- ☐ Imferon Dosage Guide
- ☐ Pocket-sized Imferon Dosage Table
- ☐ All of the above

Name _____

Address _____

City _____

State _____

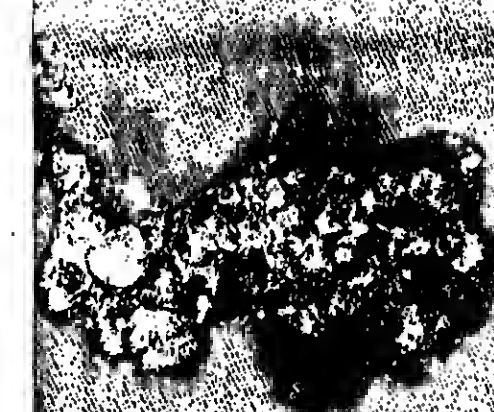
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Milwaukee, Wisconsin 53201



Plain skull film, left, of patient with cerebral paragonimiasis. Numerous multiple congregated round or oval cystic calcifications throughout right temporooccipital area are shown. Above, lateral view of same patient. Eating raw or improperly cooked host crab or crawfish causes human infection.



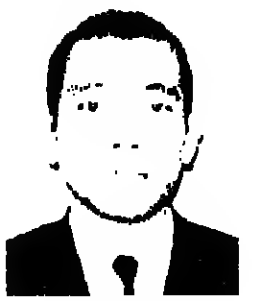
Cystoid tumor. A large number of Paragonimus ova can be seen in cystic cavity under capsule. Disease is also found in South America, Africa.



Opening of dura, above, in another patient reveals entire right occipital lobe to be completely replaced by a conglomerate of numerous granulomatous and cystoid lesions. Left, the removed tumor from right occipital lobe. Gliosis tissue connects the granulomatous with the cystoid lesions.



Ovum of the parasite as seen in smear preparation of puslike substance within the cystic cavity.



DR. MORIOKA



DR. AOKI



DR. HIROSHI



DR. TATEBAYASHI



DR. SAKATA

Cerebral Infestation By Lung Fluke Studied

A COMMON NEUROSURGICAL PROBLEM in Korea, Japan, Taiwan, and the Philippines is cerebral infestation by the lung fluke, Paragonimus westermani. Ten patients were examined by Drs. Hisashi Morioka, Hideo Aoki, Kenichiro Higashi, Kinichiro Tatebayashi, and Yozo Sakata, of Yamaguchi University Medical School, Ube, Japan.

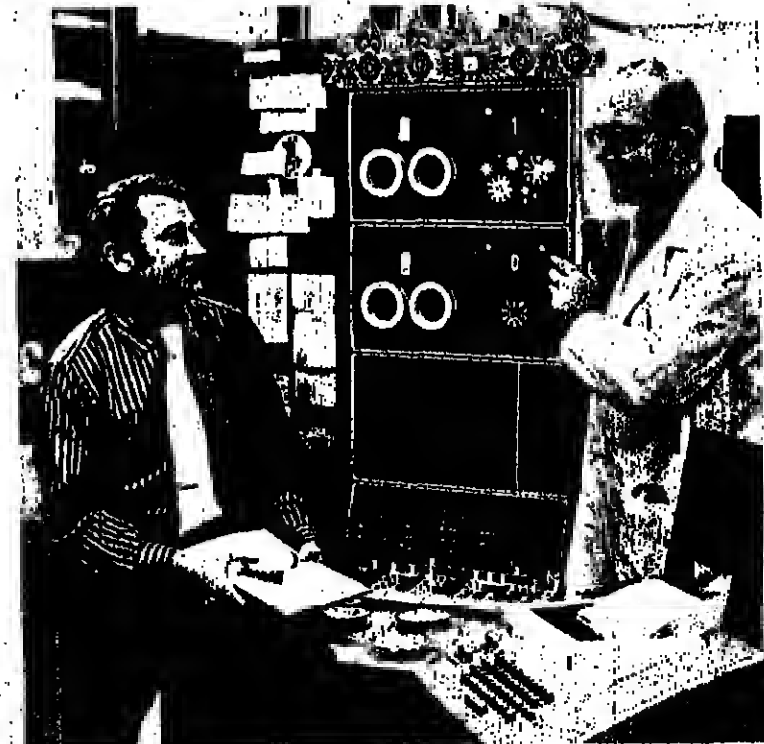
Initial neurologic symptom usually was an epileptic fit. Homonymous hemianopia was found in 80 per cent of cases. Though a majority had a vestige of pulmonary infection demonstrable in chest films, there was an active pulmonary lesion in only one case. Characteristic x-ray finding was intracranial calcification. Pneumography indicated ventricular filling, deformity, and enlargement. Skin screening test for parasite showed positive intracutaneous reaction in all five patients tested.

Making history:

A computerized questionnaire for recording medical histories has been formulated by a team headed by W. E. Hammond, Ph.D., biomedical engineer (I), and Dr. H. K. Thompson, Jr., biochemist, at Duke University Medical Center. The culmination of six years' research, it is 19 pages long and takes an average of 45 minutes to complete. There are 800 possible responses, but most patients will be required to answer only 200-250. The print-out organizes data under general history, family medical history, and review of systems.



S: Nutritional and genetic studies on arteriosclerosis included in new specialized research center at Bowman Gray. It was established by five-year NHLI grant. Director M. J. and Hugh Lofland, Ph.D., check squirrel monkeys.



'A Lot More Work' Necessary Before Human VD Vaccine Use

Continued from page 1

able to human beings, we're going to have to ensure its purity from rabbit tissue contamination."

"That last matter is of considerable concern because rabbit testicular debris in a vaccine for human beings poses possibilities of unwanted immunologic events, even including the risk of engendering a man's antibodies to his own testes."

Some other troublesome aspects of syphilis vaccine in the current state of development include the vaccine's conferring a reaction to the serologic tests now used to detect the disease. Depending on the route of vaccine administration, rabbits have turned up positive to some or all of the antibody tests now commonly used—reactions that have been found to linger as long as a year.

Also there is "no convincing evidence," Dr. Miller said, to show whether syphilis immunity is a mechanism of the humoral system or the cell-mediated system. There are some implications supporting cellular immunity, but nothing that could be considered unequivocal.

Syphilis vaccine experimental successes have been reported at least as long ago as 1967, by Dr. John M. Knox, of Baylor University, and more recently by Dr. Miller and Dr. Mieczyslaw Metzger, of the Polish Academy of Science in Wroclaw.



Dr. NORINS

Gonorrhea Incidence Climbing; No Reliable Serologic Test

From CDC, Atlanta, Ga.

► The investigation situation in gonorrhea is only slightly brighter, said the other co-chairman of the workshop here, Dr. Leslie C. Norins, of the Center for Disease Control in Atlanta, Ga.

While the estimated U.S. incidence of gonorrhea is climbing to 2,000,000 cases a year (as compared with 600,000 reported, which is a 15 per cent rise over the preceding year), there still is no reliable serologic test for the disease as there is for syphilis.

A variety of existing serologic tests suffer from the use of "crude antigens," Dr. Norins said, and the most sensitive tests

also incur the highest incidence of false positives—up to 20 per cent.

Neisseria gonorrhoeae is known to share antigens with other, apparently harmless Neisseria species and probably with other gram-negative bacteria and even with Escherichia coli, he said, making "the problem of apparent false-positive reaction one of the most vexing at this time."

One possibility for sharpening both diagnostic and therapeutic procedures against N. gonorrhoeae is raised in the electron-micrographic work of Danish investigators who have found apparent structural differences between colonies of the organism that are virulent and colonies that are not.

Dr. Alice Reyn, of the State Serum Institute in Copenhagen, told the workshop that the virulent types are accompanied by bundles of fibrils that are not seen in the field of view with nonvirulent types. Although no indisputable connection between the fibrils and the cell wall has been established, she reported, "we still feel that the fibrils most closely resemble the fimbriae (or pili) of gram-negative rods... [and] it is possible that the fibrils may play some part in the virulence of the gonococcus."

Coinvestigators included Dr. A. E. Jephcott, now at the Public Health Laboratory, Sheffield, England.

Natural immunologic response by circulating antibodies to gonorrhea infection is well recognized, Dr. Norins said, but the defense mechanism has recently been found to go beyond that. CDC investigators have identified secretory IgA antibody to gonorrhea in vaginal washings of infected subjects. And preliminary experiments indicate secretory IgA is in the urethral secretion of males with gonorrhea.

In each instance, as the mechanism of secretory antibody is understood now, that immune mechanism is independent of circulating antibody production and thus

Radiologist Appointed



University of Chicago has appointed Dr. Alexander Gottschalk as chairman of the Department of Radiology at the Pritzker School of Medicine. He has been on the faculty since 1964.

offers another possibility for enhancement of natural defenses.

While all the recent findings about gonococcal antigen and immune responses conceivably could aid the development of a vaccine against gonorrhea, Dr. Norins said, the only known approximation to a vaccine is a gonococcal autolysate prepared by investigators in Ottawa. Injected into volunteers, it stimulated a serum antibody response, but a booster dose a year later did not elicit a booster response, possibly because of antigenic fading during the year's storage.

For gonorrhea researchers, the handicap of lacking an animal model of the disease may be easing with the recent accomplishment at CDC of infecting chimpanzees (MEDICAL TRIBUNE, July 7). Urethral exudates of male patients were inoculated into the urethra of male chimps, who then infected female chimps in the customary way. The female chimp infection, asymptomatic as in many women, appears to be self-limited and subsides after about eight weeks, Dr. Norins said.

Detoxifying Study May Aid War on Pollution

Continued from page 1

natural toxicants have coexisted for eons of time. We could benefit by capitalizing on knowledge of the means by which organisms adapt to and detoxify these substances. This same general type of approach has been used to control polio, tetanus, and other infectious diseases. The etiologic agents still exist, but specific parts of the detoxification system have been reinforced sufficiently to deal with exposures. This approach, which has been so successful in microbiology, just might be helpful in toxicology."

As an example of such an approach, the investigator described an experiment in which ingestion of phenobarbital decreased toxicity from lead. The physical appearance of lead-fed rats was improved, impairment of body weight gain was virtually eliminated, and storage of lead in liver tissue was decreased 39 per cent by phenobarbital, he said.

Proof of Iodine Lack Needed Before Supplementing Diet

From NIAMD

► There is no justification for recommending iodine supplementation to any U.S. population group unless it can be shown by appropriate clinical and field studies that iodine deficiency exists, the meeting was told by Dr. Robert L. Vought, chief of the Metabolic Diseases Epidemiology Unit, Epidemiology and Field Studies Branch, National Institute of Arthritis and Metabolic Diseases.

Recently collected data strongly suggest

that we have an iodine "surfeit" in this country, he said. Probably because of heavy consumption of dairy and vegetable products, iodine intake from food alone is entirely adequate for most of our population, he added.

The average daily consumption of milk and fresh leafy vegetables alone contains 116 micrograms of iodine, or more than the 100 micrograms deemed sufficient by the National Research Council, Dr. Vought said, and over-all intake of iodine is from two to seven times the minimum.

"Unfortunately, the quantity of excess iodine needed to induce mild hypothyroidism is not known, and there is undoubtedly much variation in amounts between individuals," Dr. Vought remarked, adding that "this is an area that deserves research attention."

Effects of Intensive Exposure To Pesticides Measured

From Medical University of S.C.

► Blood pressure, plasma cholesterol, and total lipids were significantly elevated in subjects intensively exposed to pesticides, compared with nonexposed matched controls, according to Dr. Samuel H. Sondifer and Julian E. Keil, of the Medical University of South Carolina.

The comparison was made between 30 volunteer pesticide workers who had intensive mixed exposure to chlorinated hydrocarbons, organophosphates, carbamate, and other pesticides and 30 controls who were individually matched to

the volunteers by age, race, sex, and physical activity.

There were a significantly greater number of pesticide-exposed subjects than controls with abnormal systolic pressure, diastolic pressure, and overt hypertension, the investigators said. Further breakdown of the data showed abnormalities clustered in the nonwhite exposed subjects.

Significant associations were found between systolic pressure, diastolic pressure, weight, and plasma DDT concentration.

While the data suggest an association between hypertension and pesticides, the nature and significance of the association are not clear, the authors said.

Bone Fracture Healing Improves With Zinc Diet Supplement

From University of Detroit

► Dietary zinc supplementation resulted in improvement in the early stages of bone fracture healing in animal studies, according to Armen Z. Mesrobian, of the University of Detroit School of Dentistry.

Fractures of the mandible were produced in a group of bonsters, and half the animals received a 1.32-mg. dietary supplement of zinc sulfate daily, he said. At four days after fracture, both groups of animals showed hemorrhage and connective tissue-healing activity, but zinc-supplemented animals had more osteoid formation.

At seven days, all the animals had well-defined connective tissue calluses, but only the supplemented animals had developed osteoid bridges uniting fractured bone trabeculae, the investigator said.

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Vitamin E	125	69
Vitamin K	140	125
Vitamin B ₁	160	125
Vitamin B ₂	150	150
Niacin (mg equiv.)	210	210
Vitamin B ₆	175	140
Folic acid	100	100
Vitamin B ₁₂	125	125
Calcium	170	140
Phosphorus	160	115
Magnesium	120	85
Iron	120	120
Iodine	220	180

*Recommended Daily Dietary Allowances (National Academy of Sciences)

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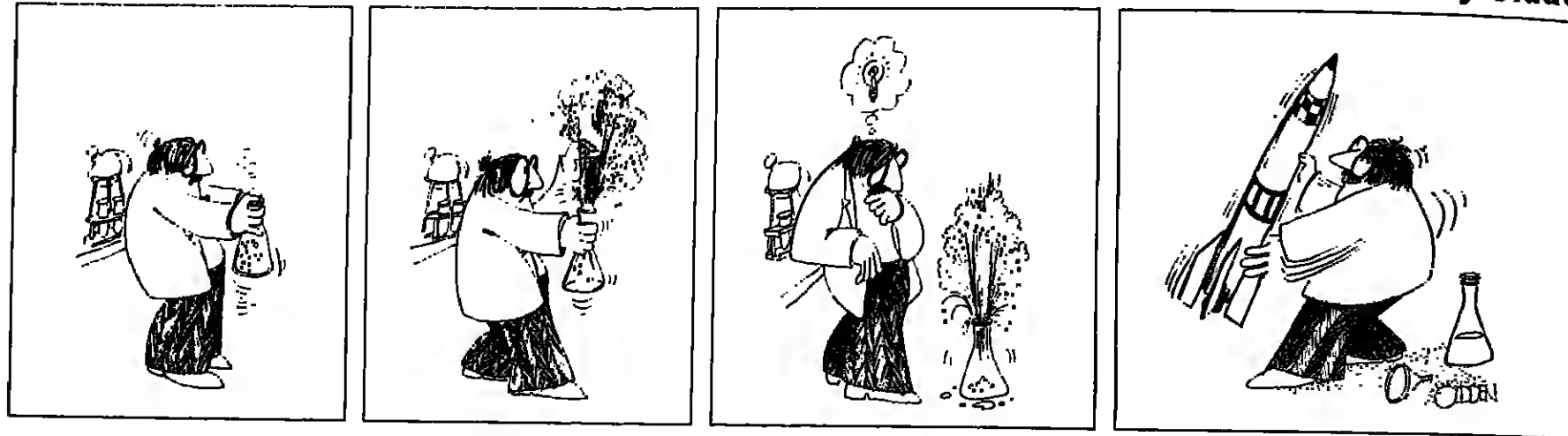
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Zero Population Growth Believed Possible in U.S. by 1980

Medical Tribune Report

SAN FRANCISCO—The United States could reach a condition of zero population growth as early as 1980, according to Donald J. Bogue, Ph.D., Professor of Sociology and director of the Community and Family Study Center at the University of Chicago.

If this condition is not attained by 1980,

it will be achieved well before the year 2000, he predicted. In 2001, the same number of births will occur as in the current year.

"In fact, white Anglo-Saxon Protestant and Jewish-American populations are already reproducing at or below the zero growth level," Dr. Bogue told a meeting of the American College of Obstetricians and

Gynecologists. Most of the country's recent slackened growth is the result of declining birth rates in minority groups whose birth rates are moderately above average, such as blacks, Spanish-speaking Americans, and Roman Catholics, he said.

Dr. Bogue attributed the decline in birth rates to:

- Expanding knowledge of contracep-

tion. "A very substantial percentage of pregnancies are still 'accidental' and undesired at the moment they occur—especially first pregnancies and pregnancies after the third child," he said. "Knowledge of contraception and access to contraceptive devices will decrease such pregnancies."

- A rise in the average age of marriage. "Older age at first marriage is linked to lower total fertility," Bogue states.
- Rapidly declining fertility of the remnants of the "high fertility culture."
- Discovery and mass availability of new and even more effective and easy-to-use methods of preventing childbirth.
- The women's liberation movement. "That working women have fewer children is widely documented. The movement will lower fertility."

Data on Cholera Used in Treating Infants' Diarrhea

Medical Tribune Report

BETHESDA, Md.—Experience gathered from epidemics of Asiatic cholera is being applied to treatment and prevention of acute diarrhea of certain American Indian infants, according to Dr. G. Donald Whedon, director of the National Institute of Arthritis and Metabolic Diseases (NIAMD).

Scientists of this institute have begun the Indian study in collaboration with colleagues from the Johns Hopkins University School of Medicine, under an NIAMD contract with the University.

Outpost Is on Reservation

The team of researchers has established an outpost on the Apache Indian reservation about 150 miles northeast of Phoenix, Ariz., at the Indian Health Service's White-river Hospital. The scientists and their families are living in trailer homes as they begin their studies among Apache Indian babies.

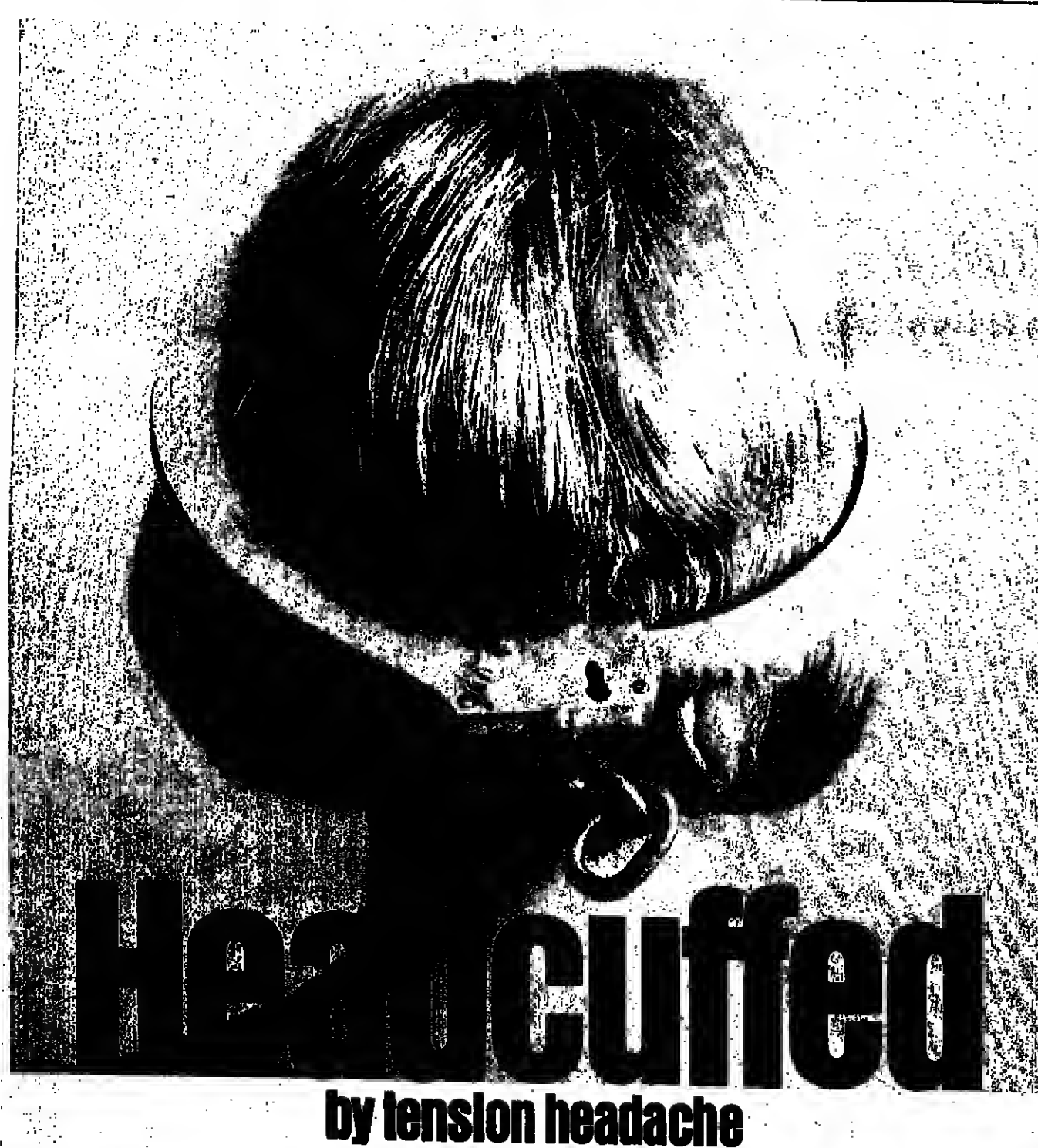
The Apache children suffer annual severe epidemics of diarrhea, and the incidence has been over one case per child per year.

The death rate, formerly very high among children under five years of age, has dropped markedly, but the disease still hospitalizes infants for long periods and causes them a great deal of suffering. It is prevalent, though less serious, among many of the other Indian tribes of the Southwestern United States, where the NIAMD is currently conducting research on arthritis, diabetes, and gastrointestinal disorders.

Dr. Robert S. Gordon, Jr., NIAMD clinical director and project officer for the study, and Dr. Norbert Hirschhorn, Assistant Professor of Medicine at Johns Hopkins, both helped to control a cholera epidemic in Dacca, East Pakistan.

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Contraindications: Hypersensitivity to any of the components.

Precautions: Due to presence of a barbiturate, may be habit forming. Excessive or prolonged use should be avoided.

Side Effects: In rare instances, drowsiness, nausea, constipation, dizziness, and skin rash may occur. Adult Dosage: One to two tablets or capsules, repeated if necessary up to 6 per day, or as directed by physician. Before prescribing, see package insert for full product information.

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CONTRAINDICATIONS: Proven or suspected pheochromocytoma; hypersensitivity to Ismelin. Do not use with MAO inhibitors.

WARNINGS: Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Warn patients not to deviate from instructions and about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during initial dosage adjustment and with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking Ismelin. Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced dosage with oxygen, atropine, and vasopressors ready for immediate use. Give vasopressors with extreme caution because patients on Ismelin may have a greater propensity for cardiac arrhythmias. Febrile illness may reduce dosage requirements. In frank congestive heart failure not due to hypertension, Ismelin is not recommended. Due to catecholamine depletion and increased responsiveness to norepinephrine, special care is required when treating patients with a history of bronchial asthma, since the condition may be aggravated.

Use in Pregnancy
The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

PRECAUTIONS: Give very cautiously to hypertensives with (a) renal disease with nitrogen retention; (b) coronary disease with insufficiency or recent myocardial infarction; (c) cerebral vascular disease, especially with encephalopathy; and (d) rising BUN levels. Give with extreme caution to those with severe congestive failure. Watch for weight gain or edema in patients with incipient cardiac decompensation. If digitalis is used with Ismelin, remember that both drugs slow the heart rate.

Appetite suppressants (eg, amphetamines), mild stimulants (eg, ephedrine, methylphenidate), and tricyclic antidepressants (eg, imipramine, nortriptyline, doxepin) may decrease the hypotensive effect of Ismelin. Wait one week after discontinuing MAO inhibitors before starting Ismelin.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver function tests are advised during prolonged therapy.

ADVERSE REACTIONS: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. Less frequently—dyspnea, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, pruritus of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (angina), chest paresthesias, nasal congestion, weight gain, and asthma in susceptible individuals.

DOSEAGE: Initial dosage should be low and increased gradually by small increments.

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C I B A

Doctor in Malawi Cites 250 Cases Of Xerophthalmia

Medical Tribune World Service
TEL AVIV, ISRAEL—About 250 children with active xerophthalmia and keratomalacia, nearly half of whom died, were seen during a three-year period by an Israeli doctor who spent three years as chief of 55-bed ophthalmologic ward at the Queen Elizabeth Central Hospital in Blantyre, Malawi. A covering corneal graft operation proved the most effective method of treatment.



Dr. BEN-SIRA

Reporting this at the eighth symposium of the Israel Ophthalmological Society here, Dr. Itzhak Ben-Sira, of the Hadassah Medical Center in Jerusalem, said the children were usually in the one-to-four age group and suffered from malnutrition, very often of kwashiorkor. The xerophthalmia and keratomalacia had been precipitated by measles, dysentery, bronchopneumonia, or chickenpox.

The children were brought to the hospital generally in an advanced stage of their disease. The cornea was either xerotic or in a state of liquefaction, often including perforation and iris prolapse. They were admitted to the pediatric department if their condition was grave, but many also received treatment in the ophthalmologic department. The patients were usually treated with antibiotics and vitamin A injection 100,000 I.U. for three days. In severe cases infusions were added. In spite of the treatment, 100 children died shortly after admission.

Graft Operation Performed

The condition of the others was too severe to perform a complicated operation, so it was decided to perform the covering graft operation. "This is a simple, very short operation and very effective," said Dr. Ben-Sira. The operation consists of cleaning the perforated corneal wound from the iris and covering it with 10.0 mm. full thickness of preserved cornea. The graft is secured by a few silk sutures far from the place of perforation. During the following month the graft seals the perforation and allows a scar to form over the perforation. The graft is removed after one month.

More than 50 such operations were performed during the three years Dr. Ben-Sira reported on, and in 45 of the eyes they were very successful. In some they resulted in small scars in front of the pupil, however, and an optical iridectomy or a real perforating graft had to be performed.

Dr. Ben-Sira said that during the three years he spent there, some 25,000 patients were received annually at the ophthalmologic outpatient department. Complicated or severe cases were admitted to the ward, the second biggest of its kind in Africa. The majority, however, were treated by local African medical assistants.

Dr. Ben-Sira and his predecessor as head of the ward, Dr. Uri Ticho, also of the Hadassah Medical Center, held training courses for the local staff, in which they were taught how to deal with the common eye diseases and to perform operations. Dr. Ticho spent 18 months at the hospital. Both doctors were sent to Africa by Prof. I. C. Michaelson, head of the department of ophthalmology at the Hadassah Medical Center, to help develop ophthalmologic services.

Immunology Training Set

FARMINGTON, CONN.—The University of Connecticut Health Center has received a \$261,684 Federal grant to train immunologists. The grant, from the National Institute of Allergy and Infectious Diseases, will support training programs to be directed over the next five years by Dr. Elmer I. Becker, Professor of Pathology.

Find Sexual Pleasure Abetted In Only 39% of Group on 'Pill'

Medical Tribune World Service

HALIFAX, N.S.—In spite of assumptions to the contrary, libidinal interest and sexual pleasure increased in less than half of a group of women using oral contraceptives who were surveyed in a Canadian experiment.

"They felt unhappy, dejected, lost appetite, weight and sexual interest, cried a great deal, had self-accusatory ideas and in some cases suicidal ruminations," he told the Canadian Psychiatric Association.

Dr. Jean N. Fortin, Professor of Clinical Psychiatry at the University of Montreal, reported here that roughly 45 per cent of the women displayed depressive symptoms while on the contraceptives.

Other, less commonly reported, side effects included dizziness, headache, and breakthrough bleeding. Dr. Fortin said. The study was carried out on 70 married women attending either private gynecologists or a community family-planning clinic in Montreal. Women with organic gynecologic illness or a history of psychiatric illness were excluded from the study. All subjects had had at least one pregnancy and had been taking oral contraceptives for at least three months.

Although some of the women had depressive states long before they started on "the pill," these states continued, improved, or became worse without any demonstrable connection with the medication.

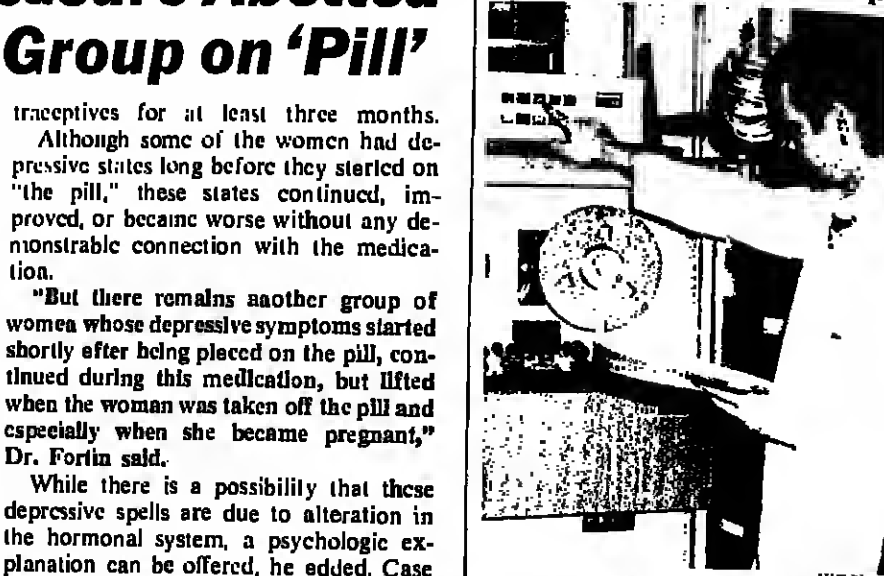
"But there remains another group of women whose depressive symptoms started shortly after being placed on the pill, continued during this medication, but lifted when the woman was taken off the pill and especially when she became pregnant," Dr. Fortin said.

While there is a possibility that these depressive spells are due to alteration in the hormonal system, a psychological explanation can be offered, he added. Case histories show that the reaction occurs in women who were reluctantly forced by circumstances to take the pill.

In addition to 38.57 per cent who reported that their sexual appetite was improved, 28.57 per cent reported their libido decreased and 32.86 per cent reported no change.

Coauthors were Eric D. Wittkower, Jacqueline Paimont, and L. Tetreault.

Trauma Registry Set Up



A computerized trauma registry has been established by researchers at the University of Illinois Medical Center, Chicago, to provide better emergency care for accident and shock victims. Hospitals in the network will be able to receive instant patient histories and clinical summaries for specific injuries. Its developer, Dr. David Boyd, checks a computer employed in the new system.

Teaching of Suicidology Is Tested With a Computerized Curriculum

Continued from page 1

data that emerged from these sessions was then digested by three sets of instruments developed for the purpose:

- Educational aims framework—a framework permitting a concise statement to be made regarding the purpose of the educational experiences for each target professional group.

- Master list of educational experience elements—this set of elements included an outline of the didactic subject material, the clinical experiences appropriate to the subject area, and such "simulated" experiences as films, tapes, plays, and so on.

- Computer algorithm—this was described by Dr. Murray as a "common sense" computer program that acted upon the set of aims stated to allocate a quota of student time to the educational experience elements.

Using these tools, the team then developed three syllabuses for each of 13 target professional groups. The syllabuses differed as to the number of hours devoted to studies of suicide and self-destructive behavior, rated as "minimum," "average," and "longer-than-average" programs.

The educational service system derived from all these steps, Dr. Resnik said, goes into action when an instructor who wishes to use it fills in a survey that tells what his educational aims are, the type of student, the classroom time available, the limitations (if any) he wishes to place on the use of special material, and the instructional mode—i.e., the theoretic orientation of the instructor himself.

Syllabus Is Generated

When these items of information are fed into the computer, a syllabus is generated that contains three items—a topical outline and approximate distribution of classroom time among topics, two sets of recommended references (one for students and one for the instructor) for each topic, and a recommended list of special materials, cross-referenced to the topics to which they relate.

In addition to these basic items, all of which are tailored to the instructor's stated needs, the package produced also contains

a narrative description of the topics included in the topical outline, a bibliography extending beyond the references specifically recommended for the program, and a list of each item of recommended special material, and an evaluation survey to be used by the instructor so that he may report any deficiencies discovered in the curricula material during its use.

The investigators reported that the program was pilot-tested last year for a cross section of disciplines. The medical school programs tested were for undergraduate medical students, psychiatric and nonpsychiatric resident physicians (including family-practice residents), and continuing education for physicians. Other groups included in the pilot programs were undergraduate and graduate nurses, master's candidates in social work, graduate sociology students, pastoral counseling students in seminaries, and mental health technician trainees in community college courses.

Dr. Resnik told *MEDICAL TRIBUNE* that word of the pilot tests at the medical schools has spread and that a number of inquiries about the program have been received.

"We're now in the process of completing our 'package,' and we hope to have them available by next winter," he said.

For Measles Study



At Georgetown University Medical Center, Dr. Joseph Bellanti examines child recovering from measles. Lymphocytes from patient's blood will be used in studying body's delayed hypersensitivity response to viruses.

Late-Onset Diabetes: Study Group Urges More Stress on Diet

Medical Tribune Report

CHICAGO—Dietary control deserves a greater emphasis in the management of maturity-onset diabetes, a meeting of the American Geriatrics Society was told here by Dr. Thaddeus E. Prout, Associate Professor of Medicine at Johns Hopkins and coauthor of the University Group Diabetes Program study.

"The results from the U.G.D.P. have given little hope that the degenerative complications of diabetes are preventable by simple control of blood glucose," he asserted.

"In the maturity-onset diabetes, neither insulin nor oral hypoglycemic agents gave greater protection against these complications than diet alone. . . . Use of additional therapeutic agents must be justified by reasons other than those of the prevention or cardiovascular complications.

"When diet alone does not provide symptomatic relief—and, in the belief of the attending physician, a lowering of blood glucose is desirable—insulin is to be preferred over oral hypoglycemic agents because it is safer.

Overzealous Use Scored

"Overzealous use of insulin in order to maintain normal glycemia and glycosuria may result in wide swings of blood glucose with repeated hypoglycemic attacks with their inherent dangers. Patients who have been vigorously indoctrinated in the need to prevent glycosuria are frequently difficult to convince that hypoglycemia is a greater danger than mild hyperglycemia. . . . Oral agents may continue to fit a need under very special circumstances. They may be used as drugs of convenience in patients with diabetes of mild to moderate severity who prove to be poorly controlled with diet and who are unwilling or otherwise unable to administer insulin."

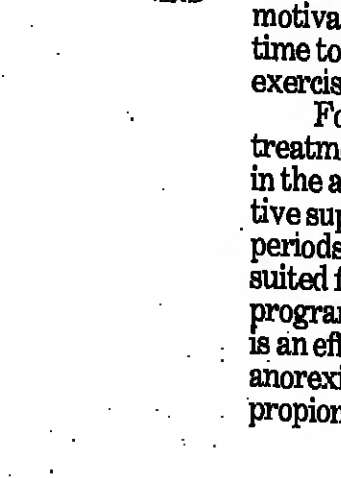
Dr. Prout remarked that "we have overworked blood glucose as a marker for this complex, multifaceted condition known as diabetes mellitus."

On the basis of available evidence, he said, we should probably conclude that elevations of blood glucose are a normal process of aging, that pathologic changes are already present at the time of diagnosis in patients with adult-onset diabetes, and that control of blood glucose by conventional standards does not give any measurable benefit as far as degenerative complications are concerned in patients with non-insulin-dependent adult-onset diabetes.

Training In Aging Funded

CORAL GABLES, FLA.—The University of Miami School of Medicine has received a five-year, \$456,006 grant extension from HEW to continue a program of training scientists as researchers and teachers in aging.

Considering a change in the way you treat obesity?



Many physicians are currently changing their approach to the treatment of the obese patient and their choice of an anorectic agent. One approach, for example, involves the increasing realization that losing weight requires patience.

Since obesity can be a serious threat to health, it should be treated by every physician. Treatment should give early motivation and give the patient time to adjust to new eating and exercise habits.

For some, this change in treatment will include a change in the anorectic used as adjunctive support during indicated periods of time. Especially suited for a total weight control program requiring an anorectic is an effective non-amphetamine anorectic like Tenuate (diethylpropion hydrochloride N.F.).

It starts right away and keeps on working.

This is demonstrated by the results of 42 clinical studies involving 1291 patients receiving diethylpropion hydrochloride.*

At the end of 16 weeks, patients achieved an average weight loss of 16.1 pounds—and they were still losing weight at an average rate of a pound per week.*



Contraindications: Concurrently with MAO inhibitors; in patients hypersensitive to this drug; in emotionally unstable patients susceptible to drug abuse.

Warnings: Although generally safer than amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease.

Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy, un-

pleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidence. As is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported in a few epileptic patients. Increased in convulsive episodes has been reported. Symptomatic cardiovascular effects reported include ones such as tachycardia, precordial pain, arrhythmia, palpitation, and increased blood pressure. One published report described T-wave

changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others. Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema. Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. Specific reports on the hematopoietic system include two cases of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been

reported by physicians. These include complaints such as dry mouth, headache, dyspnea, menstrual upset, hair loss, muscle pain, decreased libido, dysuria, and polyuria.

Abuse: Relatively few instances of substitution of diethylpropion hydrochloride for amphetamine or related drugs have been reported in the literature.

Convenience of two dosage forms: Dospan® tablets: One 75 mg. continuous release tablet daily, swallowed whole, in morning, 25 mg. tablets: One 25 mg.

tablet, three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Use in children under 12 years of age is not recommended.

*A projected weight loss curve was generated from a regression analysis of individual weight change in patients with obesity uncomplicated by hypertension, cardiovascular disease or diabetes. Duration of treatment, regimen and individual weight changes varied substantially.

†For chemical, pharmacological, and clinical differences between amphetamines and diethylpropion hydrochloride, please write to MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215.

References: 1. References and data on file, MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215. 2. Comprehensive Drug Abuse Prevention and Control Act (Public Law 91-617, 84 Stat. 1863, October, 1970).

MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215.

Merrell

World Registries Seen Key to Cancer Studies

Continued from page 1

still others by private individuals. The registries cooperating with the agency include one in Ibadan, Nigeria; one at Hamburg, West Germany (an unusually old one—it started in 1927); and another in East Berlin. Others are in Gliwice, Poland; Cali, Colombia; Kingston, Jamaica; and Ljubljana, Yugoslavia. There are also registries in Hawaii, Sweden, Japan, India, Canada, and elsewhere. One of the best and oldest, dating from 1935, is run by the Health Department of the State of Connecticut, according to Dr. C. S. Muir, head of the department of epidemiology and biostatistics at IARC.

Good Registries in Scandinavia

"There are very good registries in the Scandinavian countries," Dr. Muir told MEDICAL TRIBUNE. "Each patient is given a number he's obliged to use, and that makes linkage easy. There are registries at El Paso, Tex., and at Alameda County, Calif., but there is trouble defining the populations at risk because people move around so much."

"There's a gap in South America, but we are supporting a registry now in Lima. In Alberta, Canada, the registry works well because the physician isn't paid for treatment he gives until he reports adequately on the case. There's a good registry in Uganda, because by a paradox it is sometimes easier to run a good registry in a place where there are few sources of care or only one. In Singapore, for instance, there is only one pathology institute and only one center for radiation therapy, so the sources of information are circumscribed."

The registries that are part of the

agency's program cover 58 populations. Their reports, which constitute a basic guide to the geography of cancer, have been collected and printed, with the aid of a computer at Queen Elizabeth Hospital, Birmingham, England, in a publication entitled *Cancer Incidence in Five Continents—Volume II*. It is distributed by the International Union Against Cancer (generally referred to as the UICC), after its French name: Union Internationale Contre le Cancer, by Springer-Verlag of Berlin, Heidelberg, and New York.

"There are really three basic levels for information about cancer distribution," Dr. Muir said. "First, there are morbidity statistics. These come to the agency mostly from the cancer registries."

"Second, there are mortality statistics. These are less complete, and of course are slanted toward fatal cases. They don't give an accurate picture of the incidence of skin cancer, for example, because relatively few people die of skin cancer. They give quite an accurate picture of lung cancer incidence, since lung cancer usually kills the victim."

A third source of information, Dr. Muir said, are figures that come from pathology and radiation therapy departments without reference to a population. "For instance," he said, "in Thailand we don't know where the patients come from. Therefore, we prefer not to try to estimate a rate, but what we can do is get an idea of the relative importance of different types of cancer."

Patterns Appear in Figures

Some patterns that appear in the figures invite attention. "But," said Dr. Muir, "when we see an increase in a particular kind of cancer, we have to ask: is it a real increase, or are the doctors just getting better at diagnosis? And there are fashions in medicine, you know."

"Sometimes, however, the changes are obviously real. Take cancer of the testis in Denmark. Its incidence has doubled in 20

years in urban areas in Denmark. I can think of an improvement in diagnosis that could explain this. It is a real across-the-board increase. But in Finland, which is next door, there has been no such increase.

"This is exciting. We do not know why it is so. But Dr. Johannes Clemmensen, at the Danish Cancer Registry under the National Anticancer League, in Copenhagen, is working on the problem. He is trying to determine if there is some difference between the habits or the environment of urban Danes and urban Finns that can explain this difference."

Lung Cancer High in Finland

Some years ago it was discovered that there was a much higher lung cancer rate in Finland than in Norway. By then the lung cancer-cigarette smoking relationship was quite well established. "But," said Dr. Alheri Tuyns, of the agency's unit of epidemiology and biostatistics, "there were two groups of approximately the same kind of people, living in the same climate, yet Finland clearly had a higher lung cancer rate. We furthermore had the impression that the Norwegians smoked cigarettes about as much as the Finns."

"It turned out," Dr. Tuyns said, "that both populations were smoking a lot. But the Finns had been smoking cigarettes for 20 to 25 years. The Norwegians started many years later."

The Norwegians have not yet caught up. Their lung cancer rate among males 50 through 54 years old is 29.5 per 100,000, according to the latest available figures. Finland's rate is 134.4 per 100,000 for the comparable group. (The Norwegian rate derives from 1964-66; the Finnish rate derives from 1962-65.)

Visitors to the agency, hearing about studies of liver cancer in Africa, or an incidence difference between Hong Kong and Singapore, or the impact on health of cigar-smoking in Thailand, sometimes ask why such studies are so scattered.

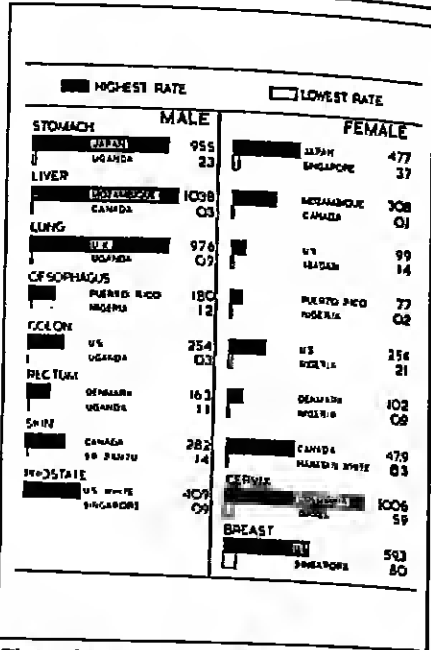


Chart denotes differences in the incidence of various cancers in selected regions. International Agency for Research on Cancer researchers say environmental agents influence disease's rate and character.

"The fact is," said Dr. Muir, "that our only hope really to look into the world of cancer is to go to places where things have not become homogenized. In England and the United States, things are homogenized. Go into a supermarket or a dozen supermarkets and you see the same foods over and over again. People eat the same things. The differences that might cause or promote cancer are in a sense covered up."

"No, we must go where the figures call us. Sometimes we are told that what we are doing is not basic enough. But what is more basic than the human being if one is interested in human disease? Perhaps it is once again becoming fashionable to consider that the proper study of mankind is man."

The next issue of MEDICAL TRIBUNE will continue this report on the International Agency for Research on Cancer.

Red Cell Transfusions Cut Sicklemic Crisis Severity

Continued from page 1

apart, for a total of 20 ml./Kg. in the two-day period. The transfusions typically raised the blood hemoglobin level an average of 4 Gm.

"While on the program, children were physically stronger, kept up with school peers, and were less slow in school," the physician reported. "Growth usually was not stimulated. . . . Severe crises became minimal in number and severity; 14 children had one or a few brief attacks of pain."

"As controls, data from these children were inhaled for one year before they entered the program, during dropout periods, and for the first month after the program stopped. Among the 30 children with adequate control observations, all had many more mild, moderate, or severe crises."

Pneumonia Seen Five Times

During the treatment period, pneumonia was seen five times in four children, acute gastroenteritis in three, mild acute hepatitis in two, and aseptic femoral necrosis in one, Dr. Ward continued. By contrast, during the control period, 14 had 30 attacks of pneumonia, four severe neutrocytosis, one aseptic necrosis of the hip, and two salmonellosis. In the first three months after the end of the trial, 13 children had a severe crisis or sickle-cell-related infection requiring hospital care.

"The greatest observation we made," Dr. Ward declared, "is that there are different varieties of the homozygous state: some are mild, some moderate, some severe. There is a great deal of heterogeneity in terms of the expression of symptomatology."

Over all, the trial suggested, he added, that prophylactic blood transfusions in these patients are "not harmful" and that there may be some children with severe disease who may benefit from the treatment, although it is not recommended as a routine therapeutic procedure.

Coauthors were Drs. I. J. Wolman and R. S. Jackson.

Adrenergic Blockade Helps Cut Stress in Diabetic Children

From University of Pennsylvania

► An ongoing trial of a beta adrenergic blocker in hyperlabile diabetic children continues to support early findings that the agent helps to prevent the effects of stress in such patients, a University of Pennsylvania investigator reported.

Dr. Robert Knye, Professor of Pediatrics, said the "encouraging preliminary results" suggest that adrenergic blockade may be useful as adjunctive treatment in the psychotherapy of these youngsters.

The trial was launched following the observation that diabetic children experienced a more rapid rise of blood ketones following epinephrine injections than normal children, Dr. Knye recalled. Following adrenergic blockade in these patients, the rates of rise of ketones, free fatty acids, and glucose were significantly reduced.

The stress-linked biochemical response was dramatically demonstrated in studies of two diabetic preadolescent girls, who were virtually incapacitated by repeated hospitalizations for severe diabetic ketoacidosis, the physician continued. In one instance, during a stress interview, a marked rise in ketones and free fatty acids was documented. In the second instance, the youngster was pretreated with the adrenergic blocker before the interview and the biochemical response failed to occur.

A subsequent regimen of oral therapy with sotalol, an investigative adrenergic blocking agent, has markedly decreased the episodes requiring hospitalization in these patients.

The study population has now been increased to 15 hyperlabile diabetic youngsters, "and encouraging results are continuing," Dr. Knye declared.

The difficulty with these youngsters is

that they are enmeshed in family stress and cannot cope with their emotional problems," he said. "Yet they tend to dissemble when they talk to a psychiatrist. They are very sweet, very pleasant, and try to hide the fact that something is wrong at home. The problem is that, unlike our stress interviews, which have an ending, the stress situation at home is a continuing one for these patients."

Recently, he disclosed, he and his collaborators have begun a pilot project of bringing in the patient's entire family for psychiatric interview. "We're finding similar stress patterns in members of the

Prostaglandins Found More Effective As an Abortifacient Than Oxytocin

Medical Tribune World Service

STOCKHOLM—Prostaglandin has become more effective than oxytocin as an abortifacient agent, Dr. Charles H. Hendricks, of the Department of Obstetrics and Gynecology, University of North Carolina, reported to a Conference on Prostaglandins in Fertility Control, organized by the World Health Organization's Research and Training Center on Human Reproduction at the Karolinska Institute here.

Dr. Hendricks said he is convinced prostaglandin has become more efficient than oxytocin despite the fact that both drugs can produce the same type of increases in the uterine contractility pattern.

The crucial difference between the two drugs is presumably some direct effect on the cervix and lower uterine segment.

Dr. Hendricks' study of E 2 and F 2A prostaglandins was part of a three-part

family in the diabetic patient," he commented. "But while the free fatty acids rise in the nondiabetic also, they soon return to normal, whereas they remain elevated in the diabetic."

He noted that treatment for these hyperlabile youngsters must have a dual aim: that of changing the pattern of emotional responses that activate biochemical factors leading to diabetic decompensation and that of protecting the patient against the consequences of the emotional turmoil aroused during the early stages of total-family psychotherapy, when the child is forced to confront his feelings openly for the first time.

Coauthors were Drs. Lester Baker, Avner Barcai, and Nasir Haque.

investigation of their effects as abortifacients—the first such investigation ever carried out in the United States. In addition to the University of North Carolina, the University of Southern California and Yale University were selected as sites for the research.

In Dr. Hendricks' study program, five women received E 2 prostaglandin in a dosage of 20 micrograms a minute and five F 2A at a dosage of 25-200 micrograms a minute. Complete infusion required 12 hours.

Of all 10 patients, only one of the F 2A group failed completely to abort. Six aborted during the initial infusion period. The mean time for complete abortion was about 18 hours for the F 2A series and 12 hours for the E 2 series.

Dr. Hendricks said he had concluded after his tests that both E 2 and F 2A were effective as abortifacients, with E 2 tending to have a higher success rate and to produce abortion in a shorter period.

Nausea and vomiting were observed more often with F 2A than with E 2, he said, but transient chemical vasculitis was seen in several patients who received E 2.

Azo for what she's aware of

(Each tablet contains 100 mg phenazopyridine HCl)

The symptoms that brought her to you. Urgency, frequency, burning—these are the discomforting symptoms of cystitis that caused the patient to seek your help. Lasting relief depends on controlling the infection. But immediate relief may call for an analgesic. This is the patient who needs Azo Gantanol®: Azo to relieve symptoms; the action of Gantanol® (sulfamethoxazole) to control the bladder infection.

Gantanol for what you're aware of

Bacterial infection

In just 2 to 3 hours after the initial adult dose, therapeutic blood and urine levels begin fighting *E. coli* as well as susceptible strains of *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis* and, less frequently, *P. vulgaris*.

She'll feel better while she gets better

As the Gantanol (sulfamethoxazole) component begins to fight the infection, analgesic Azo starts to relieve symptoms associated with bladder inflammation and irritation. For symptomatic cystitis, prescribe Azo Gantanol to help your patient feel better while she gets better.



Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Important Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. **Contraindications in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.**

Warnings: Safe use in pregnancy has not been established, and teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity

reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis, a frequently dose-related reaction, may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: Blood dyscrasias: agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; **allergic reactions:** erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; **gastrointestinal:** nausea, emesis, abdominal pain, hepatitis, convulsions, ataxia, hallucinations, dizziness, vertigo and insomnia; and **miscellaneous reactions:** drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some gottogens, diuretics (acetazolamide and thiazides)

and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infection is 4 tablets initially, then 2 tablets morning and evening. If pain persists beyond seven days, causes other than infection should be sought. After relief has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl, bottles of 100 and 500.

In acute, nonobstructed cystitis

Azo Gantanol®

(Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.)

B.I.D. therapy for the symptoms, for the infection

Roche Laboratories, Division of Hoffmann-La Roche Inc., Nutley, N.J. 07110

New Method Devised for Determining Virulence in Strains of Streptococci

Medical Tribune Report

BETHESDA, Md.—Georgetown University scientists, in research supported by the National Institutes of Health, have found a new method of distinguishing between harmful and harmless strains of streptococci.

"The method offers an additional test for evaluating virulence in the streptococci and possibly other organisms," Robert I. Krasner, Ph.D., a visiting professor in the Departments of Pediatrics and Microbiology, said.

His assistants were Linda M. Taylor and Mei C. Yeng.

The method used was a modification of the nitroblue tetrazolium dye test, a procedure used to detect chronic granulomatous disease of childhood. The researchers mixed the dye in test tubes with two groups of streptococcal strains and white blood cells taken from normal subjects. The

dye, a yellowish color, is reduced to formazan, which shows up as a blue-black compound.

"The greater the intensity, or darkness, of the dye, the greater is the stimulation of the white blood cells," Dr. Krasner said. "This results from the cells' ingesting the bacteria and then killing them."

"We found that the avirulent strain [of streptococci] is taken up and killed by the white blood cells as evidenced by reduction of the dye. The virulent strain... is resistant to ingestion by the white blood cells."

Dr. Krasner emphasized that the research is preliminary. "Its present value is in the study of properties of bacteria that contribute to infection," he said.

Dr. Krasner is Professor of Biology at Providence College, Rhode Island. He has been studying at Georgetown in the division of pediatric virology.



White blood cells are examined by Dr. Krasner in study of streptococci virulence.

Book Aims at Better Judgment In Use of Diagnostic X-Ray

Medical Tribune Report

WASHINGTON—The genetically significant dose from medical diagnostic x-ray procedures "can be significantly reduced" by implementing present recommendations for x-ray beam restriction, the Food and Drug Administration's Bureau of Radiological Health and the American College of Radiology declare in a newly published booklet.

The booklet, designed to improve professional judgment in the use of diagnostic x-ray procedures and to increase patient and user protection, says that in some instances "as much as two-thirds of the present exposure may not contribute to diagnostic information and therefore may be unnecessary."

Nearly 500,000 copies of the booklet are being distributed to physicians, medical students, podiatrists, veterinarians, and radiologic technologists.

Empiricism Urged in Finding Cause of Cancer

Medical Tribune World Service

BURTON, ENGLAND—A switch to the empiric approach could help provide conclusive proof, much more quickly than can laboratory investigation, that a human tumor is caused by a virus, in the view of M. A. Epstein, Professor of Pathology at Bristol University.

The proof might best be obtained by producing a vaccine against the suspected virus and administering it on a large scale to see if the incidence of the carcinoma decreases, says Professor Epstein, who in 1964 helped to isolate the virus associated with his name.

The Epstein-Barr virus could be the first proved to be carcinogenic in man. The virus was first discovered in 1964 in cells cultured from Burkitt's lymphoma, a tumor of children which is endemic in certain areas of Africa and New Guinea.

Since then there has been accumulating evidence, indirect and circumstantial, that the virus is the causative agent of the lymphoma, said Professor Epstein, in a Medical Tribune interview.

Once the safety and efficacy of a vac-

cine had been proved, it could be given to children in areas where Burkitt's disease is endemic. If protection against EB virus results in a drop in the expected number of tumor cases, then some sort of causal relationship will have been demonstrated.

Since the peak incidence of the tumor in children is at the age of five, the experiment could be completed within five years or "10 at the most," says Professor Epstein.

"There are a lot of people who will regard this vaccination approach to the problem as heresy," says Professor Epstein. "They will say, 'You can't go and put a potential cancer virus into people. And how would you grow it? It only grows in malignant cells and it's not safe to use.' There are enormous problems—how potent vaccine was prepared in 15 years. It only took eight years to make rubella vaccine and only five to make a measles vaccine."

The present indirect evidence that EB

virus is the cause of Burkitt's lymphoma is strong, he says. The virus is known to be a stimulator of lymphoproliferation. It can confer the power of unlimited growth in vitro on normal human lymphocytes, which ordinarily will not grow in tissue culture. It is also responsible for the in vivo lymphoproliferation of infectious mononucleosis.

Recently a herpes virus has been shown to induce a fatal lymphoreticular tumor on inoculation into both owl monkeys and marmosets. A herpes virus indistinguishable from the EB virus, has been proved to cause Marek's disease, a lymphomatous syndrome of chickens, says Professor Epstein. Furthermore, a vaccine has been made which protects the chickens against the disease.

Despite all this evidence, it is possible that in human beings the EB virus may be no more than an "opportunistic passenger, living as a commensal in lymphoid cells, particularly where there are hyperactive or proliferative disease states."

It takes a few minutes to review.

Clinical and bacteriologic responses of patients with skin and soft tissue infections treated by 55 investigators with Cleocin HCl (clindamycin HCl hydrate, Upjohn)*

Infection	No. of Patients	Pathogens	Clinical Response		Bacteriologic Response	
			Excel. or Good (%)	Poor (%)	No. of Pts. Evaluable	Organisms Eradicated (%)
Abscesses, wounds, & furuncles	156	<i>S. aureus</i> - 107 staph, other- 12 <i>β-strep</i> - 10	151 (97%)	5 (3%)	129	126 (98%)
Cellulitis	38	<i>S. aureus</i> - 21 staph, other- 1 <i>β-strep</i> - 8	38 (100%)	--	30	30 (100%)
Superficial skin & soft tissue—mostly impetigo	183	<i>S. aureus</i> - 41 Mixed <i>β-strep</i> & ataph - 51 staph, other- 1 <i>β-strep</i> (74 Group A) - 81	178 (97%)	5 (3%)	174	170 (98%)
Total	377	-----	367 (97%)	10 (3%)	333	326 (98%)

*Data on file, Medical Research Files, The Upjohn Company

Note: With *β*-hemolytic streptococcal infections, treatment should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

Some strains of staphylococcus resistant to clindamycin HCl have been recovered. Therefore, as with all antibiotics, *in vitro* susceptibility studies should be performed.

97-100% of patients with susceptible skin and soft-tissue infections (staph and strep) had excellent to good response with clindamycin HCl.

Each preparation contains:
150 mg. Capsules 150 mg.
75 mg. Capsules 75 mg.

Cleocin (clindamycin, Upjohn) is a new semisynthetic antibiotic produced from the potent compound lincomycin and provides more *in vitro* potency, better oral absorption and fewer gastrointestinal side effects than the parent compound.

Cleocin HCl (clindamycin HCl hydrate) is indicated in infections of the upper and lower respiratory tract, skin and soft tissue, and, adjunctively, dental infections caused by gram-positive organisms which are susceptible to its action, particularly streptococci, pneumococci and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

CONTRAINDICATIONS: Patients previously found to be hypersensitive to this compound or to lincomycin.

WARNINGS: Safety for use in pregnancy not established. Not indicated in the newborn infants below 30 days of age.

PRECAUTIONS: Prescribe with caution in atopic individuals. Perform periodic liver function tests and blood counts during prolonged therapy. The serum half-life in patients with markedly reduced renal function is approximately twice that in normal patients; hemodialysis and peritoneal dialysis do not effectively

remove Cleocin from the blood. Therefore, with severe renal insufficiency, determine serum levels of clindamycin periodically and decrease the dose appropriately. Should overgrowth of non-susceptible organisms—particularly yeasts—occur, take appropriate clinically indicated measures.

ADVERSE REACTIONS: Generally well tolerated in clinical efficacy studies. Side effects reported in 8.2% of 1,414 patients. Of the total, 6.9% reported gastrointestinal side effects and 1.3% reported other side effects. Diarrhea or loose stools were reported in 3%. Gastrointestinal symptoms included abdominal pain, nausea, vomiting and diarrhea or loose stool. In a few instances, diarrhea lasted for several days; one case of bloody stools was reported. Hematopoietic: Transient neutropenia (leukopenia) and eosinophilia have been reported; relationship to therapy is unknown. No irreversible hematologic toxicity has been reported. Skin and Mucous Membranes: Skin rash and urticaria have been reported infrequently. Hypersensitivity reactions: A few cases of hypersensitivity reaction have been reported. If hypersensitivity occurs, discontinue drug and have available the usual agents (epinephrine, corticosteroids, antihistamines) for emergency treatment. Liver: Although no direct relationship of Cleocin HCl (clindamycin HCl hydrate) to liver dysfunction has been noted and significance of such change is unknown, transient abnormalities in liver function tests (ele-

vations of alkaline phosphatase and serum transaminase) have been observed in a few instances. Also, abnormal liver function test values at the beginning of therapy have returned to normal during therapy.

ADVERSE REACTIONS: Generally well tolerated in clinical efficacy studies. Side effects reported in 8.2% of 1,414 patients. Of the total, 6.9% reported gastrointestinal side effects and 1.3% reported other side effects. Diarrhea or loose stools were reported in 3%. Gastrointestinal symptoms included abdominal pain, nausea, vomiting and diarrhea or loose stool. In a few instances, diarrhea lasted for several days; one case of bloody stools was reported. Hematopoietic: Transient neutropenia (leukopenia) and eosinophilia have been reported; relationship to therapy is unknown. No irreversible hematologic toxicity has been reported. Skin and Mucous Membranes: Skin rash and urticaria have been reported infrequently. Hypersensitivity reactions: A few cases of hypersensitivity reaction have been reported. If hypersensitivity occurs, discontinue drug and have available the usual agents (epinephrine, corticosteroids, antihistamines) for emergency treatment. Liver: Although no direct relationship of Cleocin HCl (clindamycin HCl hydrate) to liver dysfunction has been noted and significance of such change is unknown, transient abnormalities in liver function tests (ele-

Notes: With *β*-hemolytic streptococcal infections, treatment should continue for at least 10 days to diminish the likelihood of subsequent rheumatic fever or glomerulonephritis.

SUPPLIED: 150 mg. Capsules—Bottles of 16's and 100's. 75 mg. Capsules—Bottles of 16's and 100's. Sensitivity Disk—2 µg. Sensitivity Powder—Viola.

For additional product information, see your Upjohn representative or consult package insert. MED 8-45 (11/69-3) 1/71-1446

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Upjohn

We'd like you to form an opinion of the clinical and bacteriological experience with 377 patients in the treatment of staph and strep soft-tissue infections* with clindamycin HCl

In our opinion, this clinical and bacteriological work points to Cleocin HCl (clindamycin HCl hydrate, Upjohn) as a drug with potential value in the treatment of staph and strep soft-tissue infections. If you share this opinion, we'd

appreciate knowing about it. And one good way of letting us know would be to ask your Upjohn representative for samples and/or additional information. Cleocin should be prescribed with caution in atopic individuals.



Cleocin HCl
clindamycin HCl hydrate, Upjohn

*Due to susceptible organisms.

Special Measures to Prevent Synthetic-Turf Injury Urged

Medical Tribune Report

ITHACA, N.Y.—Prophylactic measures should be taken to prevent "the larger and deeper abrasions occurring notably on synthetic turf," according to Dr. Alexius Rachun, Professor of Clinical and Preventive Medicine and team physician at Cornell University.



DR. RACHUN

Long-sleeve jerseys, extra padding about the joints, and full-length stockings should be worn by athletes playing on such a surface, he advised.

He observed that, in addition to dermatitis resulting from bacterial, fungal, and viral infections, vexatious and, at times, disabling skin problems among athletes originate from mechanical, iatrogenic, and allergic factors.

Among the mechanical factors, other than synthetic turf, that cause skin lesions, he said, is faulty athletic gear.

"Protruding rivets and bolts in football helmets and hurried or missing cleats with exposed prongs occasionally inflict skin wounds to the wearer or to others," said Dr. Rachun. "Routine checks on athletic apparel should include a survey for these defects."

He further observed that avulsion may occur when fingernails and toenails are

not kept short and that infected ingrown toenails arise from the pressure of tight shoes.

One source of iatrogenic lesions, he pointed out, is the treatment room, where inept or careless use of heat modalities may result in local skin burns.

Proper Training Straasand

"Prevention," Dr. Rachun said, calls for the employment of therapists trained in the proper use of the modalities. The athlete under their care should be attended throughout treatment, which should be stopped whenever complaints of excessive heat over the treated area are made.

Skin irritation from tightly applied tape also fall within the iatrogenic category, he said. These are usually minor friction burns and commonly occur about the ankle in the area of the Achilles tendon and on the dorsum of the foot, he noted, adding that ulcerated lesions with secondary infections do occasionally develop.

"Gauze padding, a dab of petrolatum, and care against drawing the tape too tightly over vulnerable areas are useful precautions in minimizing or preventing these lesions," he remarked.

Among the iatrogenic skin problems, Dr. Rachun included burns due to exposure to quicklime "injudiciously" used in stripping playing fields.

"Scrupulous attention on the part of athletic administrators and grounds-keeping personnel should be observed in ensuring the use of lime of safe composition," he said.

Discussing the allergic category, Dr. Rachun said that contact dermatitis occurs with "moderate frequency." Sensitivity to tape, as opposed to simple mechanical irritation, sometimes presents a problem to both the athlete and the trainer, he noted. In known cases of sensitivity, he suggested that a protective layer of gauze or similar material be applied between the skin and the tape, and he suggested that nonallergic tape, usually too costly for ordinary athletic budgets, be used sparingly over bare skin areas to secure a firm strapping.

Tincture of benzoin compound applied to skin as an adherent prior to taping is a more common source of contact sensitivity, and he recommended the use of suitable substitutes containing rosin, which have been found to be less sensitizing.

Physician Cycles to Work



Finishing last leg of 4-mile bicycle trip is Dr. Donald Eltzman, Professor of Pediatrics, University of Florida College of Medicine, Gainesville. Dozens of physicians at the center travel to and from work by pedal power.

"The dermatitis resulting from the topical application of some antibiotic ointments, soaps, and mercurial antiseptics," he added, "can be eliminated by the use of carefully selected substitutes having a low index of sensitivity."

Blue Cross Unit To Give Coverage For Outpatients

Medical Tribune Report

DAYTON, OHIO—A three-month trial of "Verticare"—providing outpatient insurance coverage—has been undertaken by Charles F. Kettering Memorial Hospital here and the local Blue Cross plan.

The program has been named Choice (for Comparative Hospital Outpatient/Inpatient Care Experiment) by the hospital's physicians and administrators who initiated the idea and developed it in conjunction with Blue Cross of Southwest Ohio and the National Cash Register Company.

To Get Outpatient Service

Under the pilot program, appropriate patients who are members of Blue Cross or of N.C.R.'s hospitalization coverage plan will receive on an outpatient basis all the necessary hospital services they might ordinarily have received as inpatients. Blue Cross or N.C.R. hospitalization coverage will pay for the services. Robert L. Willett, associate hospital administrator, said:

"If we can accomplish treatment of

health problems while the patient is still 'vertical'... it will save time and money for the patient, the hospital, the patient's health-care program, and ultimately the public....

"The Verticare idea, put into practice nationwide, could take much of the pressure off overcrowded hospitals.... It might even reduce the number of additional hospital beds required to serve many cities in the future."

Dr. Harold Fishman, a member of the Kettering medical staff who helped formulate the plan, said:

"The program ends a real struggle of conscience for the physician. Often we find a family that will face real financial hardship if a course of treatment is undertaken in such a way that insurance will not pay."

"In the past, our only recourse has been to order the patient admitted to a hospital, even though admission may not have been absolutely required from a medical standpoint."

"With the economic pressure relieved by Verticare, the doctor can be a lot more objective about tying up hospital beds and services."

Purely diagnostic tests, physical examinations, and clinic visits are not covered by the program.

A.M.A. Is Planning to Set Up Liability Insurance Program

Medical Tribune Report

CHICAGO—A professional liability insurance program, to be established initially in four in seven states by 1972, was announced here by the American Medical Association.

The program will not interfere with group insurance plans that state medical societies now have in operation in 24 states, the A.M.A. said.

One of the program's key features is peer review, which will permit members of a medical society to refuse to admit into the program those deemed by their colleagues to be unacceptable or representing a high liability risk.

Educational Efforts Emphasized

The program will emphasize educational efforts, including seminars, workshops, lectures, manuals, and periodic bulletins, to inform physicians of the causes of malpractice claims and to work with them on methods of eliminating these causes, the A.M.A. said.

In addition to peer review, individual medical societies also will participate in writing terms of the insurance policies, in

evaluating claims, and in day-to-day administration of the program.

Worked out by the A.M.A. with the CNA Financial Corporation, which operates the Continental Casualty Company and the Continental Assurance Company as subsidiaries, and the brokerage firm of Marsh & McLennan, Inc., the program is aimed at easing the cost and increasing the availability of malpractice insurance.

Provisions of the plan include predetermined rates for the first three of the program's five years, based on regional actuarial experience and socioeconomic trends; guaranteed renewability as long as peer review requirements are met; and profit-sharing incentives.

The insurance offered has been designed in two layers.

The basic layer, up to \$100,000, encompasses the smaller but more frequent claims. This will be available on a cost-plus basis in which the society's own loss experience will be a major factor in computing the final cost, based on a prearranged rating formula.

If this layer of coverage is operating on a profitable basis, members will receive a credit reflecting income from the premium collected for this \$100,000 layer of coverage.

Coverage up to \$1,000,000 will be provided on a traditional insurance basis. A further \$4,000,000 may be available to applicants meeting certain additional eligibility requirements.

CNA said it intends to make 75 per cent of the gross premium dollar available for claims and claim expenses. In contrast to the 55 to 60 per cent of most liability policies, Economy will be brought about, it said, through mass marketing and computerization.

Through the use of a computer data bank, rating structures, claim information, and program operations can be monitored daily, CNA said.

Particulars of Plan Given

Under the plan, CNA will establish three to five programs in four to seven states. Each program will operate at the state or county level with an administrator selected by the local medical society. No physician will be dropped from the plan without consent of his medical society.

The program "breaks new ground" and "is, for me, a very satisfying occasion," commented Dr. Carl Hoffman, president-elect of the A.M.A. and chairman of its Committee on Professional Liability.

"The fact is that medical malpractice claims have risen nearly 50 per cent over the past five years," he said. "These claims are increasing at a rate higher than the general inflation in our national economy."

The new A.M.A. program was announced at a press conference headed by Dr. Hoffman. Other participants were Jacques W. Sammet, president of Continental Casualty and Continental Assurance, and Newell P. Weed, Jr., executive vice-president of Marsh & McLennan.

The fundamental approach is the new program, Mr. Sammet summed up, "is one of a risk-control system, rather than the traditional transfer of risk."

"This means a joint effort to pinpoint the causes of claims and reduce their chance of recurring," he said. "It means a closely coordinated program of legal, claim control, and other loss prevention techniques."

Hospital's Operating Cost Up

NEW YORK—The cost of operating New York Hospital climbed from \$32,000,000 in 1965 to \$62,000,000 in 1970, according to the annual report. Factors cited in the increase included a rise in the yearly compensation of interns from \$3,500 to \$10,500, a rise in the starting salary for registered nurses from \$4,500 to \$9,420, and a rise of 278 per cent in the salaries of the resident staff during the five-year period.

Severity of Injuries To Ankle Graded More Easily the Next Day

Medical Tribune Report

BOSTON—Grading the severity of ankle injuries in athletes can be done more accurately a day after rather than immediately after the injury, according to Dr. Thomas B. Quigley, of Howard Medical School.

"What may appear as a trivial sprain immediately after injury, with minimal pain, tenderness, and edema, may have become severe and disabling when examined after 24 hours," he said. "Occasionally, an apparently severe sprain will, after a day of treatment, be found to be of only moderate or minor degree."

"The most common ankle injury, a grade 2 sprain of the anterior tibiotalar and tibiocalcaneal ligaments, if seen immediately after injury and treated, should be restored to full athletic activity eight to 10 days after injury."

Sprain Graded by Severity

The degree of ankle ligament sprain can be graded in severity from 1 to 4, Dr. Quigley said. Grade 1 is the least degree of ligament stretch that may be considered to be a sprain, 2 is the most common, 3 is a severe sprain with the ligament still in continuity, and grade 4 is a complete rupture or avulsion of the ligament.

"A golden opportunity for definitive diagnosis of ligament rupture or avulsion is present for about half an hour after injury," he said. "Gentle, diagnostic manipulation reproducing the mechanism of injury during this period, before edema and spasm have developed, is not uncomfortable."

Treatment of ligament sprain in the absence of fracture, suggested Dr. Quigley, should include cold, compression, rest, and elevation for the first 24 hours. After that, heat and gentle massage may be applied.

Dr. Quigley said that surgical repair is better than immobilization for cases of rupture or avulsion of the deltoid ligament. On the other hand, primary repair need rarely be done for rupture of the fibular collateral ligament, and surgical repair of a rupture of the anterior tibiotalar ligament is not necessary.

The Cold Truth about



Stuffy Noses and Coughs

Children do well with an oral decongestant

Topical decongestants work fast, but don't go far enough. They don't shrink all the nasal and sinus tissues.

Rondec S oral decongestant shrinks mucous membranes and blocks histamine response

Shrinking mucous membranes from the tip of the nose down to the bronchi, pseudophedrine is apparently more specific than ephedrine for the vessels of the respiratory tract. But it has fewer side effects. Pressor action is minimal. Significant CNS stimulation is rare. It doesn't cause rebound congestion or irritation.

Carbinoxamine has a high level of antihistamine activity. And while sedation may occur, it is generally mild and transient—shouldn't give a school-age child that wooden-headed feeling.

Rondec-DM adds cough control that's non-narcotic

The dextromethorphan hydrobromide in Rondec-DM controls unproductive cough without the constipation and respiratory depression associated with narcotics. Drowsiness or gastrointestinal upsets rarely occur. And glyceryl guaiacolate works to thin bronchial secretions.

Two products for dependable relief of cold symptoms. Two good flavors kids like. And a low incidence of side effects.

That's the long and short of it.

cut cold symptoms down to size

for stuffy noses: Rondec S[®] Syrup

50 mg pseudophedrine HCl and 2.5 mg carbinoxamine maleate per 5 ml

for cough with a cold: Rondec-DM[™] Syrup

15 mg dextromethorphan HBr, 100 mg glyceryl guaiacolate, 50 mg pseudophedrine HCl, and 2.5 mg carbinoxamine maleate per 5 ml



How Supplied: Rondec S Oral Drops is available in 20 ml bottles of black currant-flavored dropper dosage. Calibrated, shatterproof dropper enclosed in the carton. Unique Spill-guard[®] closure prevents spilling when dropper is removed from bottle. List No. 183.

Rondec S Syrup, black currant-flavored, is available in 15 fl oz (1 pint) bottles. List No. 185.

Rondec C Chewable, scored tablet with Tutti-Frutti flavor, is available in bottles of 100. Each tablet marked with Ross R and List No. 181 for professional identification.

Rondec T Tablet is available in bottles of 100. Each tablet marked with Ross R and List No. 180 for professional identification.

Rondec-DM Drops is available in 20 ml bottles of grape-flavored dropper dosage. Calibrated, shatterproof dropper enclosed in the carton. Unique Spill-guard[®] closure prevents spilling when dropper is removed from bottle. List No. 186.

Rondec-DM Syrup, grape-flavored, is available in 15 fl oz (1 pint) bottles. List No. 187.

Rondec DSCAT and Rondec-DM are available on prescription only.

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COLUMBUS, OHIO 43260
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carbinoxamine maleate. However, it is generally mild and tolerance appears to develop rapidly in most cases. Patients particularly sensitive to antihistamines may experience moderate or severe drowsiness.

Mild gastrointestinal disturbance and drowsiness have been observed among patients receiving dextromethorphan hydrobromide or glyceryl guaiacolate. These instances are rare, and no serious side effects have been reported.

Patients should be cautioned to exercise care in driving or operating machinery until the possibility of drowsiness is determined. If a sensitivity reaction or photosensitivity should occur, reduce dosage or withdraw the drug.

Administration and Dosage: Clinical trials among series of infants and children indicate that the usual dosage frequency of four times daily is effective and well tolerated. Because response to the ingredients will vary according to the illness and type of patient under treatment, dosage should be adjusted by the age and clinically determined needs of the individual patient. In mild cases, dosage and/or frequency may be reduced.

There is no known contraindication to the use of Rondec S and T or Rondec-DM as adjunctive therapy to antibiotics when relief of mucosal congestion and cough is desired.

Precautions and Side Effects: Although pseudophedrine causes virtually no pressor effects in normotensive patients, use with caution in hypertensives. While the majority of patients will experience no side effects from pseudophedrine hydrochloride, those particularly sensitive to sympathomimetic amines may note mild stimulation.

Sedation has been observed in connection with the use of

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Sedation has been observed in connection with the use of

Avoid the complications of "diuretic overdry"

With Esidrix diuresis is gentle yet prompt. No one denies there's a time and place for a highly potent nonthiazide.

But most patients rarely need it. Which is why hydrochlorothiazide—originated by

CIBA as Esidrix—remains the most widely used oral diuretic.

With Esidrix you usually avoid the abrupt flushing out common with fast-acting nonthiazides.

Diuresis is prompt; edema is relieved gradually over a 12-hour period. Which is usually fast enough. Just as important, it's smooth and gentle.

Moreover, the risk of serious salt and water loss is reduced.

However, since fluid and electrolyte imbalance may occur, patients should be watched closely for clinical signs (please see brief prescribing information).

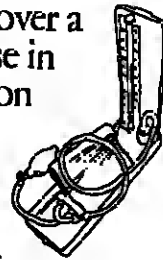
Things are complicated enough for the edema patient. Rely on Esidrix, the smooth, gentle diuretic. Particularly in maintenance therapy.

Proven by over a decade's use in hypertension

Esidrix is still unsurpassed as a diuretic-antihypertensive. Labeling for one newer nonthiazide states: "Hypertensive patients who cannot be adequately controlled with

thiazides will probably also not be adequately controllable with [furosemide] alone."

And Esidrix is amply proven alone in mild hypertension. As an adjunct in mild to severe cases.



Esidrix®
(hydrochlorothiazide)
is often just enough



Dorothy Lamour—star of stage, screen and television.

Esidrix® (hydrochlorothiazide)

Indications: Edema and hypertension. Contraindications: Anuria; known drug allergy to thiazides or other sulfonamide-derived drugs.

Warnings: Small bowel stenosis, with or without ulceration, has been associated with use of osmotic cathartics. Thiazides may accelerate development of hepatic coma. Do not give to patients with known allergy to thiazides or other sulfonamide-derived drugs.

Patients with renal disease, thiazides may precipitate azotemia. Cumulative effects may develop in those with impaired renal function. Dosage should always be carefully titrated. Pay special attention to electrolyte balance of patients with severe hepatic insufficiency. In patients with cirrhosis and ascites, watch for symptoms of impending hepatic coma (confusion, drowsiness, tremor) and test for increased serum ammonia concentration, sodium and potassium excretion. Thiazides may decrease glucose tolerance; use cautiously in diabetics. Hypokalemia may occur but is generally reversed by a uricosuric agent. Thiazides may decrease renal responsiveness to natriuretic hormones and increase responsiveness to tubocurarine; if possible, withdraw therapy 2 weeks prior to surgery. Hypotensive episodes under anesthesia have been observed. If emergency surgery is indicated, pre-anesthetic and anesthetic agents should be administered in reduced dosage. The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma.

Use in Pregnancy: Thiazides should be used with caution in pregnant or lactating patients since this drug crosses the placental barrier and appears in breast milk and may result in fetal hyperbilirubinemia, thrombocytopenia, or altered carbohydrate metabolism. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

Precautions: Perform serum potassium, BUN, uric acid, and blood sugar tests prior to and at appropriate intervals during therapy. Watch patients for clinical signs of fluid or electrolyte imbalance (hypokalemia, hypochloremic alkalosis, hypotension). Warning signs: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pain or cramps, muscular fatigue, hypotension, oliguria, tachycardia, GI disturbance. Serum and urine electrolyte determinations are particularly important when patients are vomiting excessively, receiving parenteral fluids, steroids, or ACTH; during brisk diuresis; in presence of severe cirrhosis.

Adverse Reactions: Gastrointestinal: anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestasis), pancreatitis, hyperglycemia, glycosuria. Central nervous system: dizziness; vertigo, paraesthesia, headache, xanthopsia. Dermatologic: hypersensitivity—purpura, photosensitivity, rash, urticaria, exfoliative dermatitis, leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia. Cardiovascular: orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Miscellaneous: muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy. Dosage: Tablets should be taken with

or immediately after meals. EDema: Initial—50 to 100 mg once or twice daily for several days. Maintenance—25 to 100 mg daily or intermittently. Refractory patients may require up to 150 mg daily. Hypertension: Initial—Usual dose 75 mg daily. Maintenance—After a week dosage may be adjusted downward to as little as 25 mg or upward to as much as 100 mg daily. In resistant patients, up to 150 mg daily may be required. Combination therapy—When necessary, other antihypertensives may be added gradually and with caution because of the potentiating effect of this drug. Dosages of ganglionic blockers should be halved. Supplied: Tablets, 50 mg (yellow, scored) and 25 mg (pink, scored); bottles of 100, 1000, and 3000. Consult complete literature before prescribing.

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C I B A

Fantasy and Medical Students at Yale

Eleven medical students who at one time fantasized a career in the arts and letters, instead of medicine, turn out to be a different breed of cat from 31 of their classmates, whose fantasized alternative careers were in science, teaching, law, or business, according to a recent study in the *American Journal of Psychiatry*.

Apparently, a little yearning is a dangerous thing if the humanities figure in the yearning. A questionnaire was sent to the 83 graduating students of the 1970 class at Yale University School of Medicine in an attempt to find out something about the problem of the alienation of today's youth, without considering what they are alienated from. The study sought to locate a dissatisfied group of medical students and define the group's characteristics. (There were 46 replies, cut back to 41 by the failure of five students to report any fantasy or to fantasy in any of the above areas. We assume them to be would-be firemen or trolley-car conductors.)

In terms of percentages, more of the 11 "dissatisfied" arts and letters fantasists than their classmates had seen psychiatrists, entertained thoughts of suicide, experienced feelings of depersonalization, failed to perceive Yale as one of the top three medical schools, majored as undergraduates "in some area subsumed under the rubric of arts and letters," attended at least one concert during the academic year, read more nonmedical books (in fact, read more books than anyone except the would-be teachers), failed to claim a religious affiliation, used marijuana (although 13 of the 30 "satisfied" students also used it), and did not intend to enter academic medicine.

The authors seem to consider these 11 students as one-down, "... more conflicted about their identity... like foreigners in a community with strong scientific emphasis," not like the rest of us chickens.

A New Englander once wrote, "... only as far as [people]... are unsettled is there any hope for them." Of course, he was a Harvard man (class of 1821) named Emerson, and heaven knows what he thought of Yale.

We wish the oames and addresses of those 11 foreigners in a scientific community had been included so we could find one in an hour of medical need or middle-aged identity crisis. The "satisfied" others, presumably, will all be teaching or busy writing love letters to Yale.

And, speaking of marijuana, we're happy to share with you the first paragraph of a letter to the editor of England's *Journal of Pharmacy and Pharmacology*:

"A disadvantage of previous methods of assaying the potency of cannabis preparations... is that they cannot be used for determining effect of cannabis in rats. One possible approach is to use the degree of ataxia or catalepsy induced by the drug, another is to use vocalization as reported by Carlini & Kramer (1965). They found that, under the influence of cannabis, rats vocalize when they are touched."

So if you hear any rats singing...

"Amidst cheers the Secretary garlanded Dr. G. K. Tyagi, following which Dr. K. M. Iel, M. Prakash, O. P. Goel and A. U. Khan paid their tributes to him. They praised the hard work and sincerity with which Dr. Tyagi developed this Medical College from a scratch."

—Journal of the Indian Medical Association.

You never know how what a scratch will develop.

Readers are invited to contribute items of 100 words or less to this column. Contributions should be mailed to MEDICAL TRIBUNE, 110 East 59th St., New York, N. Y., 10022.

Tribune Economic Analysis

Two Major Blunders Cited In Freezing Wages, Prices

By ELLIOTT J. KATZ
Publisher of Tribune Service

THE "SPRITS OF 'MID-TWENTY' MILLS, the chairman of the House Ways and Means Committee, is not only good business for Nixon. It is the only business left for him to try to get into. But Mills is not in the business of "stunt" politics—any more than Chun En-hai is. Looking backward at the flash-in-the-pan promise of Nixon's last stunt, his China play, it threatened to turn into a fiasco when the economy started to collapse. Looking forward to the even more sensational dramas of his new stunt, it was born of panic and formalizes his new status of dependence on House Ways and Means Committee Chairman Mills. This new political stunt will work as well as the economic performance measuring up to it, and Chairman Mills has the measuring rod.

Overkill is the problem—as it generally is when overdefensiveness gets in the way of generosity. Not being in politics myself, I feel inclined to allow myself the luxury of one vehement "I told you so" in derision of all the cliché artists and slogan mouthers who have been giving me a hard time for sounding the alarm.

Indebted to Chairman Mills

As for Nixon, because he is in politics, he would have been in much better shape—preparatory to triggering the biggest buying panic in American stock market history, in the worst situation in American financial and economic history—if he had taken the high road and acknowledged his debt to the creditor he now has no alternative but to satisfy—namely, Chairman Mills. Indeed, if he had done so, he might have managed to have his speech writers do a better job of borrowing Mills' entire program instead of forgetting a basic ingredient—namely, cash tax rebates for export earnings.

In my formulations, I never went further than to reiterate that the "hands off" labor policy had been bankrupt as a policy and an invitation to national bankruptcy ever since the General Motors strike of 1970 and to urge the President to make the Government a party to key wage negotiations in the public interest. Rushing into a wage-price freeze is as reckless an expression of extremism as refusing to go so far as jawboning was in the first instance. It is the economic policy-making equivalent of dropping an atomic bomb where reconnoitering with an appropriately armed helicopter would have been sufficient.

90-Day Clause a Blunder

The edict about wage-price controls would have been more formidable as a threat. I regard the 90-day clause as Nixon's first blunder. His second was the decision to waste 30 of the 90 days by giving Congress a vacation. It does not seem to me that critics of the present Administration are less than competently plagiarized without being consulted, a stretch-out of present three-year labor contracts into a four-year term—with upcoming monthly cost-of-living and annual pay increases deferred—would have been less foolhardy or provocative.

"Wilt and see" is the biggest single danger posed by the 90-day emergency freeze. If business buying and consumer spending respond to the Administration's announcement that it means to wait and see for 90 days by doing the same, the panic will come back on just as if the President had not bought time by making his move. As a practical matter, the 90-day clause became academic on day one. Everyone expects it to be extended.

The headaches are here—right on the heels of the first hurries in the headlines. If "wait and see" turns out to be the general reaction of the consuming public—specifically, if consumers wait to see how long it takes for the fact of overkill to replace the fear of unemployment—the automatic beneficiaries of the new deal will be... manufacturing more troubles than

Named Dean at Stanford



Appointed dean of the Stanford University School of Medicine and Vice-President for Medical Affairs is Dr. Clayton Rich. He was at the University of Washington School of Medicine.

couraged. It is an illusion. The fact is that the central banks of the dollar-evolver countries are being forced to buy dollars in order to prevent their export products from being priced up and out of a shrinking market. The dollar crisis is being overestimated by the opinion makers, who were also underestimating the domestic panic. Up to now, had quotes for the exchange value of the dollar in Europe have been the price of strengthened American bargaining power in Europe. But America has been looking bad while doing better. Connally is moving to call Europe's bluff with gold near the top of its trading range.

Many patients react to being told how sick they are by taking off on a big spree. The stock market has a long rocky road to travel back to health. Meanwhile, the initial response of the stock market is proof positive that the Burns philosophy and the Mills plan will be trusted to work end, moreover, will work—if only the White House will let itself be shown how. The market is worth a markup for effort and a markdown for execution.

Mayo Clinicians to Study Clinical Atherosclerosis

Medical Tribune Report

ROCHESTER, MINN.—A new coordinated research program in clinical atherosclerosis has been launched at Mayo Clinic under a five-year, \$2,100,000 grant from the National Heart and Lung Institute.

The Mayo research facility will be termed a Specialized Center of Research, a program developed by the National Institutes of Health.

The major activities of the Mayo project will be conducted within the division of cardiovascular diseases by a 40-man team under the direction of Dr. H. N. Coleman.

Among the research highlights will be a study of the role of cholesterol and related sterols in the disease, an attempt to relate the patient with certain abnormalities to atherosclerotic disease, and a program to screen 5,000 school-age youngsters to determine the incidence of elevated cholesterol in children.

MEDICAL MEETING SCHEDULE

Foreign Meetings

- Oct. 18-21 ... European Congress of Allergology, Marseille, France
- Oct. 19-22 ... Bolivarian Congress of Endocrinology, Caracas
- Oct. 20-26 ... Pacific Dermatology Association, Guadalajara, Mexico
- Oct. 21-29 ... International Congress of Aviation and Space Medicine, Tel Aviv
- Nov. 11-14 ... Asia Pacific Congress on Diseases of the Chest, Taipei
- Nov. 19-20 ... Norwegian Otolaryngology Society Annual Meeting, Oslo
- Nov. 19-22 ... Congress of the Asian and Australian Society of Neurological Surgeons, Tokyo
- Nov. 21-25 ... Conference of Latin American Medical School Faculties, Montevideo, Uruguay
- Nov. 22-26 ... Asia-Pacific Congress of Radiology, Melbourne, Australia
- Nov. 28 ... World Congress of Psychiatry, Mexico City
- Nov. 29 ... International Congress of Surgeons, Western Hemisphere Congress, Panama City
- Oct. 18-21 ... American Society of Plastic and Reconstructive Surgeons, Montreal
- Oct. 19 ... International Symposium on Family Planning in Health Services in Socialist Countries, Rostock, East Germany
- Oct. 19-16 ... American Urological Association, San Francisco
- Oct. 19-17 ... American Urological Association, Guadalajara, Mexico
- Oct. 19-18 ... Latin American Cancer Congress, Caracas
- Oct. 19-17 ... General Medical Association for Psychotherapy, Munich, West Germany
- Oct. 17-18 ... International Fertility Association Congress, Tokyo
- Oct. 17-25 ... World Congress on Fertility and Sterility, Tokyo and Kyoto
- Oct. 18-21 ... International Federation for Hygiene, Preventive Medicine, and Social Medicine Congress, Madrid

Medical Tribune

and
Medical News

In Two Sections, Section 1
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world news of medicine and its practice—fast, accurate, complete

Wednesday, September 22, 1971
Vol. 12, No. 37

"Big boys don't cry"



At least seventy-five out of one hundred adults with duodenal ulcers are men.¹ Certain stress patterns may explain why.

Men start defending their masculinity at an early age. A mother admonishes her son that "big boys don't cry" because crying is the negation of everything our society thinks of as manly. It may be particularly significant that studies of patients with duodenal ulcer have revealed them generally to be craving recognition and especially vulnerable to threats to their manly assertive independence.²

Alvarez³ observes that many a man with an ulcer loses his symptoms the day he shuts up the office and starts out on vacation. The problem is, the type of man likely to have an ulcer is the type least likely to take long vacations or take it easy at work.

Still, the stress factor must be dealt with.

And here is where the dual action of adjunctive Librax can help. It's the only drug that combines the antianxiety action of Librium® (chlordiazepoxide HCl) with the antisecretory/antispasmodic action of Quarzan® (clidinium Br).

The action of Librium reduces anxiety—helps protect the vulnerable patient from over-reaction to stress. At the same time, the action of Quarzan helps quiet the hyperactive gut, decreasing hypermotility and hypersecretion.

Librax: It can't change man's nature. But it can usually make it easier for men to cope with the discomfort of stress—both psychic and gastric—that can precipitate and exacerbate duodenal ulcer.

Librax: Rx #60 1 cap. t.i.d. a.c. and 2 h.s.

References: 1. Silen, W.: "Peptic Ulcer," in Wintrobe, M. M., et al. (eds.): *Harrison's Principles of Internal Medicine*, ed. 6, New York, McGraw-Hill Book Company, 1970, p. 1444. 2. Wolf, S., and Goodell, H. (eds.): *Harold G. Wolff's Stress and Disease*, ed. 2, Springfield, Ill., Charles C Thomas, 1968, pp. 68-69. 3. Alvarez, W. C.: *The Neuroses: Diagnosis and Management of Functional Disorders and Minor Psychoses*, Philadelphia, W. B. Saunders Company, 1951, p. 384.

end tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies

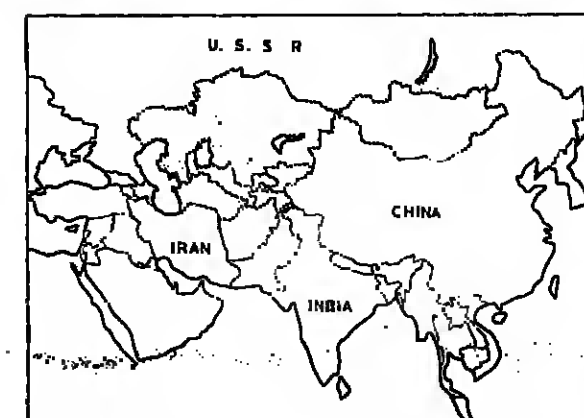
in the treatment
of duodenal ulcer
adjunctive
Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br.

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Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically. Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extensor plantar symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

On the Trail of Cancer in Iran



Near Gomishan, Iran, above, Dr. Jenez Kmet (facing camera), of the IARC, is trying to uncover the factors causing high incidence of esophageal cancer in the region. Left, map shows distribution of the disease in Asia. The belt ranges from north of Korea through Mongolia, large sections of the Soviet Union and northern Iran and terminates in Turkey.

Unit Traces Esophagus Cancer By Study of Alcoholic Drinks

LYON, FRANCE—Intriguing odors come from the anonymous brown bottles on the labeling bench in a laboratory at the International Agency for Research on Cancer here. One bottle unmistakably contains rum and another one vodka. A third holds a measure of distilled cider.

But the bottles are out for any kind of celebration. The scientists at Lyon are more interested in the carcinogens they may contain than in their alcohol content. The purpose is to investigate the many puzzling variations in the etiology and incidence of esophageal cancer, an inquiry that is being conducted in both hemispheres.

In France, an area of high incidence, cancer of the esophagus has been usually linked with excessive consumption of strong alcoholic drinks, tobacco having a synergistic role. But comparative studies by IARC experts of different regions in France throw doubt on the absolute nature of this link. And in Iran, another area of high incidence, alcohol and tobacco do not seem to play a significant role.

The IARC is also following the behavior of the disease in other parts of Asia, in the Soviet Union, in Ceylon, and in the Caribbean.

"There is always a pattern in cancer, but the pattern for cancer of the esophagus is very disconnected," Dr. J. A. Tuyns, of the IARC department of epidemiology and biostatistics, told *Medical Tribune*. "It may be the only type of cancer where differences in mortality vary by a ratio as much as one to 50. Mortality from cancer of the esophagus is 50 times higher

Scan of Liver Less Specific Than Supposed

Medical Tribune Report
LOS ANGELES—The sensitivity of the liver scan in cancer patients has been frequently noted, but its lack of specificity has not been sufficiently emphasized, a meeting of the World Federation of Nuclear Medicine and Biology was told here.

Experience with 63 patients with histologically proved cancer indicates that the value of this procedure in patients with cancer is limited, according to Drs. Joseph A. Volpe, Robert J. Lull, and Martin L. Nusynowitz, of the Nuclear Medicine Service at William Beaumont General Hospital, El Paso, Tex.

Results of the liver scan and histologic studies done within six months of the scan agreed in 56 of 63 cases, they said. Of the 46 cases in which the scan was compared with autopsy findings, the correlation was positive in 44.

Scan and biopsy correlated in 12 of 17 cases, but this relatively poor agreement cannot be attributed only to inaccuracy of the scan, since negative biopsy results are frequently erroneous, the physicians said.

In 22 cases of proved liver metastases, bilirubin, serum glutamic oxaloacetic transaminase, and alkaline phosphatase were measured, and all three of these tests were normal in seven cases, a false-negative incidence of 32 per cent. All 22 cases showed an abnormal scan.

The three tests were also normal in six of 16 patients with autopsy-proved non-tumor liver pathology, a false-negative incidence of 37.5 per cent, and again all 16 had abnormal scans.

The liver scan cannot be used as a gauge

Continued on page 14

Hospital Group Backs Nixon On the Freeze

Medical Tribune Report
CHICAGO—Delegates of the American Hospital Association, suddenly finding their organization working in behalf of President Nixon's wage-price freeze, voted to endorse the economy-shrinking move.

But even the A.H.A. president had to concede at the annual convention here that "we don't know yet what it will mean to hospital economics—we're expecting a lot more guidelines than we have now."

Two days later, the 700-bed Wesley Memorial Hospital here began firing employees in a move to reduce the payroll by 12 per cent. A spokesman said the hospital was "caught in a bind on contracts because now we can't raise our rates."

The A.H.A. involvement in the freeze was announced on the eve of the convention by its executive president, Dr. Edwin L. Crosby. He said the U.S. Office of Emergency Preparedness had asked the association to serve as a clearinghouse for information concerning the effects of the freeze on the nation's hospitals and other health care institutions.

The A.H.A. president, Jack A. L. Hahn of Indianapolis, told a news conference that he saw the job as one "to make sure the hospitals know the OEP policy and serve as liaison" during the 90 days of the initial freeze imposed by President Nixon.

Continued on page 14

Automated Ultrasound Device Detects Pre-eclamptic Women

Medical Tribune Report
PHILADELPHIA—An automated ultrasound blood-pressure instrument has proved more accurate than clinic personnel in detecting pre-eclampsia heralded by hypertension, a Howard University team reported here to the National Medical Association. Detailing the findings in 38 pregnant patients at a prenatal clinic followed through delivery, the team said that the ultrasound instrument noted blood pressures in 10 cases at least 20 mm. Hg systolic and 10 mm. Hg diastolic higher than that observed by the admitting nurse.

"Of these, two cases were clearly hypertensive, according to the instrument, and were recorded as clearly normotensive by the admitting nurse. Both were admitted within two days with pre-eclampsia and obvious hypertension," said Dr. Augustus Godette, Fellow in Obstetrics-Gynecology.

He added that the device, an Arteriosonde blood-pressure instrument (ABPI), also "monitored blood pressures accurately throughout" therapy in a series of patients with eclampsia, postpartum hypertension, persistent hypertension, or hemorrhage. The monitoring proved to be a useful guide to treatment, "helping to alert staff to 'overhoot' in drug therapy."

In undertaking the study, Dr. Godette said, he and Dr. John F. Clark, Professor

Continued on page 17

Convulsions in Cholera Patients May Follow Magnesium Reduction

Medical Tribune World Service
VITTEL, FRANCE—The abrupt onset of convulsions in patients undergoing fluid therapy for cholera may be due to a sudden reduction in plasma magnesium, it was suggested here by Dr. Akio Kobayashi, specialist in nephrology and gastroenterology at the National Children's Hospital, Tokyo.

Dr. Kobayashi told participants in the first International Symposium on Magnesium Deficit in Human Pathology that hypomagnesemia had been found to occur consistently after the initial rehydration of cholera patients. This phenomenon reversed the hypermagnesemia which was observed prior to treatment. During the 24 hours which followed initial rehydration of the patients, the magnesium deficit continued to increase, with various choices of fluid and electrolyte treatment. Normal plasma values were found again in the course of convalescence.

He warned against the conclusion that the hypermagnesemia observed at the outset indicated a sufficiency of the Mg ion, since it was primarily a measure of the severity of dehydration. Thus, the administration of fluids revealed the underlying deficiency. Convulsions, coma and other central nervous system complications in cholera patients were especially common in the pediatric age range.

"Clinical experience has shown that intravenous magnesium sulfate is frequently efficacious in treatment of convulsions," Dr. Kobayashi said.

During an epidemic of El Tor cholera, plasma and fecal magnesium levels were

measured in 59 patients admitted to the San Lazaro Hospital in Manila, the Philippines, he reported. The patients were randomly divided into four groups. The first group received both initial rehydration and maintenance therapy with lactated Ringer's solution. The second group was given lactated Ringer's solution for initial rehydration and thereafter received maintenance therapy with a solution including sodium, potassium, chloride and lactate. The third group had initial rehydration and maintenance treatment with physiologic saline. The fourth group was given lactated Ringer's solution with the oral administration of 10 per cent potassium citrate.

In all patients the plasma magnesium levels were elevated at the time of admission. The mean level in children patients from one to six years of age was 2.68 mEq/L of plasma as compared with a normal level for this age of 2.41 mEq/L. High concentrations were also found in all other age groups.

Three hours after rehydration was begun, Dr. Kobayashi said, the values were "drastically reduced under the normal in all groups . . . observation at the end of 24 hours showed further reduction of the concentrations."

The degree of reduction in plasma magnesium was greatest in the third group of patients, treated with physiologic saline and sodium bicarbonate. The deficit was greatest of all, following initial rehydration, in two children who suffered from convulsions.

Mass X-Ray Exam Seen More Useful Than Symptomatology in Lung Cancer

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NEWS INDEX

Diagnosis

Automated instrument proves accurate in detecting pre-eclampsia . . . 1

Immunization

Cervical vaccine preferred against rubella in women of childbearing age . . . 1

Radiology

Liver scan's lack of specificity in cancer patients is stressed . . . 1

Medical Groups

Hospital association votes to endorse Nixon's wage-price freeze . . . 1

CLINICAL NEWS NOTE: "Clinical experience has shown that intravenous magnesium sulfate is frequently efficacious in treatment of abrupt onset of convulsions in patients undergoing fluid therapy for cholera." (Dr. Akio Kobayashi, specialist in nephrology and gastroenterology at the National Children's Hospital, Tokyo; see above.)

Ob/Gyn

Oral contraceptives may induce migraine in some young women . . . 3

Research (3,16)

Armadillo is found to be satisfactory model for study of leprosy . . . 3

Pharmacology

HRV devising test to assess efficacy of drugs used for depression . . . 5

A Briefing in Manila



Yellow fever is extremely rare in Asia, but health authorities remain extremely wary because the Aedes aegypti mosquito has a wide distribution. In Manila, Amador Corredo (r.), of the Philippines Quarantine Service, apprises a physician of its characteristics.

Philippines Lacking MDs; Ceylon Acts on Shortage

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MANILLA—A "brain drain" is rapidly depleting the supply of physicians in the Philippines.

More than 9,320 practicing physicians have left the country, according to a study by Dr. José Cuyegkeng, executive director of the Association of Philippine Medical Colleges.

Of these, 5,720 are permanently lost, having established residence abroad with no intention of returning to their country.

The remaining 3,600 are temporarily out of the country and will eventually return, the study revealed.

COLOMBO—The Government has taken emergency steps to halt a serious loss of doctors to foreign countries. The action has been taken at a time when the country is facing the threat of a major outbreak of poliomyelitis, among other health problems.

The first measure was to impose an immediate and total ban on the departure of physicians to take jobs abroad. The only exceptions will be made for those who had signed contracts before May 12 of this year.

At the same time, Prime Minister Sirima Bandaranaike has directed an appeal to Ceylon's doctors already working in other countries to return.

Finally, the Government is considering the abolition of an examination given by the Educational Council for Medical Graduates that qualifies doctors for practice in the United States.

About 200 doctors—more than half the annual output of Ceylon's two medical colleges at Colombo and Peradeniya—left the country last year, so officials told MANILA TRIBUNE.

More than 70 left during the first half of the current year, and there is a large backlog of applications.

It Is Still a Problem, But Tapeworm Rate Declines in Finland

Medical Tribune World Service

OULU, FINLAND—Two decades ago one in every five persons in Finland had tapeworm; now the rate has fallen to one in 20, but the worm still represents so important national health problem.

Changed eating habits and improved hygienic and sanitary conditions are largely responsible for the drop in the incidence rate. Details of the battle being carried out against diphylobothriasis were given at the second International Symposium on Circumpolar Health here by Dr. W. Nyberg, of the Minerva Institute for Medical Research in Helsinki.

He said some worm carriers develop a manifest megaloblastic anemia now known to be a vitamin B₁₂ deficiency state. Describing research into this condition, he said Diphylobothrium latum acts on the B₁₂-intrinsic factor complex, releasing the vitamin from its bound form. Most of the liberated B₁₂ is then taken by the worm and not the host. One in 50 worm carriers develops a manifest megaloblastic anemia and 51 per cent have abnormally low serum B₁₂ values.

Although the detailed mechanism by which the worm splits the B₁₂-intrinsic factor complex is not known, there is some evidence that the worm contains an as yet unidentified factor capable of releasing the bound vitamin.

Dr. Nyberg described clinical studies in which radioactive B₁₂ was given orally to tapeworm carriers. When a B₁₂ absorption test was performed, it was found that both smemic and nonemic worm carriers absorbed significantly less B₁₂ than controls. This pointed to the fact that D. latum, even in nonemic carriers, impairs the absorption of vitamin B₁₂ by its host.

"The consequences of the latent B₁₂ deficiency of nonemic worm carriers are not yet fully understood," he declared, "but it is worth mentioning that some of these patients develop neurological eye lesions."

Swimming Pools Store Water in Kenya Cholera Emergency

Medical Tribune World Service

NAIROBI—Kenyan officials have hit on a new way of fighting cholera—by using portable swimming pools as emergency water tanks.

When the recent cholera alert began, portable pools were flown from Nairobi to many outlying areas where the inhabitants normally rely on rivers and lakes for their drinking water. Water was pumped into the pools, treated to kill bacteria, and then drawn off again through a plastic pipe for drinking and washing.

Water-borne infection dropped sharply in areas where the emergency tanks were installed, officials reported.

FEATURE INDEX

In Consultation . . . 5
Chess Problem . . . 9
Cartoons . . . 9, 11, 16
Editorials . . . 11
Letters to Tribune . . . 11
Epigram . . . 14
Medical Report . . . 21
Medical Meeting Schedule . . . 21
Sports Report . . . 23
Immateria Medica . . . 23

Coming next issue: see page 5

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Wednesday, September 22, 1971

MEDICAL TRIBUNE

Migraine Linked To Contraceptive In Some Women

Medical Tribune World Service

ELLSBORO, DENMARK—Oral contraceptives can bring out a latent tendency to migraine headache in some young women, and the correlation is even more marked when there was a previous history.

Clinical evidence of this, including a danger of thrombosis with permanent damage to the nervous system, was presented here by Dr. J. Desmond Carroll, consultant neurologist at the Regional Neurological Unit, Guilford, Surrey, England.

Dr. Carroll based his findings on studies made on two groups of women taking oral contraceptive pills. The first group consisted of 215 patients who had attended his clinic over a period of three years and who, prior to taking the pill, had never complained of significant headache. The second included 75 consecutive patients at the migraine clinic in whom there was a typical history of migraine headaches before being put on the pill.

Two Headache Types Present

In all, 70 women (32 per cent) in the first group experienced headaches. These included 48 whose headaches were generalized and of a vague type and 22 (10 per cent) with lateralized headaches that were apparently of the vascular migrainous type.

"It is clear in this analysis," Dr. Carroll told an International Headache Symposium here held under the sponsorship of the American Association for the Study of Headache and the Danish Migraine Society, "that in 10 per cent of these patients the pill brought out an inherent susceptibility to migraine, but more often in those who had a family history of headaches or allergic disorders."

Despite the fact that many patients stopped taking the pill, this did not produce a complete remission of migrainous headaches in all cases.

Among the 75 patients in the second group, 37 reported a deterioration in their migraines that took the form of an increase in either frequency or severity or both.

A high proportion also noted a distinct change in the pattern of their attacks. In a few patients, focal symptoms accompanied the migrainous headaches for the first time.

Twenty-nine patients reported no change in the pattern of their migraines and nine reported a distinct improvement, especially in the degree of severity.

Opposite Results Reported

In the discussion following delivery of Dr. Carroll's paper, Dr. Per Olef Lundberg of Sweden pointed out that he had achieved opposite results to those of Dr. Carroll in a study on a larger, nonselected series.

Whereas Dr. Carroll's patients came from headache clinics, Dr. Lundberg's patients were taken from a contraceptive pill clinic.

Dr. Lundberg, who is Assistant Professor of Neurology at the University Hospital in Uppsala and president of the Swedish Migraine Society, encountered 228 women who had previously suffered from migraine among a total of 1,676 requesting prescriptions for the pill.

Following consumption of various oral contraceptives for a median period of one year, 66 of the women who had had migraine suffered still worse from the affliction, but 129 of them experienced an improvement. This indicated an overall favorable effect from the consumption of oral contraceptives.

Since the number of different drugs used in Dr. Lundberg's study was so great, it was impossible for him to determine which constituents had the most favorable effects.

However he suspected that the high-progestogen pills were superior to the high-estrogen ones.

Armadillo May Provide Model For Investigation of Leprosy

Medical Tribune Report
Washington Bureau

WASHINGTON—Research scientists at the U.S. Public Health Service Hospital, Carville, La., and the Gulf South Research Institute, New Iberia, La., have succeeded in transmitting lepromatous leprosy to an armadillo and believe that they have found a satisfactory animal model for investigation of the disease.

The work was reported at a press conference here by Dr. Waldemar F. Kirchheimer, chief of laboratory research at Carville, and co-workers, in cooperation with Dr. Eleanor E. Storrs, of the Gulf South Research Institute.

Dr. Jack Butler, PHS director of hospital, described it as "a significant advance that could lead to control or eradication of leprosy."

An earlier technique for growing leprosy bacilli in the footpads of mice, he noted, is limited in its applicability by the fact that the infection does not spread beyond the site of the injection and the animal must be severely altered to maintain the infection.

The Carville team succeeded in giving

leprosy to an armadillo injected with 18,000,000 live bacteria taken from a patient in Norman. In February, 1970—a year after the injection—the armadillo manifested clinical signs of leprosy, developing large sores on both ear lobes, the injection site. Five months later the animal died—surprising the investigators, since the disease rarely kills human beings.

Tissue studies, Dr. Kirchheimer said, showed that the infection site contained about 20 billion bacteria for each gram—"five times as many bacteria as have ever been found in man." This suggests that the armadillo—or at least this particular animal—may be more susceptible to leprosy than man, he observed.

Investigators believe, Dr. Kirchheimer said, that armadillos will provide the long-sought acceptable animal model. They live long enough to get the disease, which in human beings may take three to five years to show clinical signs, he noted.

It has been noticed, he said, that only a few members of a particular animal species are susceptible to infection with bacteria resembling leprosy bacilli, and he therefore expects that no "as yet unknown



Leprosy has been transferred to a nine-banded armadillo, similar to one examined by Drs. Waldemar F. Kirchheimer (l.) and John Trautman, who is director of the USPHS Hospital, Carville, La.

proportion of experimentally infected armadillos will be susceptible and hence will develop the progressive form of the disease."

Dr. Kirchheimer speculated that the armadillo's unusual reproduction characteristics—it breeds easily and gives birth every time to a litter of four identical twins—might make it possible "to breed from a set of lepromatous parents, fully susceptible armadillo populations."

1962 was a bad year for Staph infection

In a hospital study from 1960 to 1967, only 2 positive staphylococcal lesions were noted among 34,262 infants washed with pHisoHex®. Both occurred in 1962.

In 6 additional studies, 24 of 1974 infants washed with pHisoHex, Staph colonization was only 2.4%; while in 1160 "unwashed" control infants, colonization amounted to 45%.

Anti-Staph protection for the infant usually begins with a pHisoHex bath before he leaves the delivery room. It can be continued and strengthened throughout the infant's stay in the hospital nursery by bathing him daily with pHisoHex and having everyone who handles the infant wash his hands with pHisoHex before and after handling the baby. This routine builds a cumulative, rinse-resistant film of antibacterial hexachlorophane on the skin to form a powerful barrier against Staph and many other bacteria.

Mothers can maintain this antibacterial protection at home by bathing baby axillarily with pHisoHex. And nonalkaline, hypoallergenic pHisoHex is kind to skin. Won't dry or irritate even when used frequently.

References: 1. Gluck, Louis: Hosp. Practice 3:33, Jan., 1968 (author's correction). 2. Payne, Margaret O.; Wood, H. F.; Karakawa, Walter, and Gluck, Louis: Am. J. Epidemiol. 82:305, Nov., 1966. 3. Gluck, Louis, and Wood, H. F.: New England J. Med. 285:1177, Dec. 14, 1967. 4. Simon, H. J.; Alwood-Pardes, Juan, and Trejos, Alonso: Pediatr. 85:254, Feb., 1965. 5. Gluck, Louis, and Wood, H. F.: New England J. Med. 285:1177, Dec. 14, 1967.

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Changed eating habits and improved hygienic and sanitary conditions are largely responsible for the drop in the incidence rate. Details of the battle being carried out against diphylobothriasis were given at the second International Symposium on Circumpolar Health here by Dr. W. Nyberg, of the Minerva Institute for Medical Research in Helsinki.

He said some worm carriers develop a manifest megaloblastic anemia new known to be a vitamin B₁₂ deficiency state. Describing research into this condition, he said Diphylobothrium latum acts on the B₁₂-intrinsic factor complex, releasing the vitamin from its bound form. Most of the liberated B₁₂ is then taken by the worm and not the host. One in 50 worm carriers develops a manifest megaloblastic anemia and 51 per cent have abnormally low serum B₁₂ values.

Although the detailed mechanism by which the worm splits the B₁₂-intrinsic factor complex is not known, there is some evidence that the worm contains an as yet unidentified factor capable of releasing the bound vitamin.

Dr. Nyberg described clinical studies in which radioactive B₁₂ was given orally to tapeworm carriers. When a B₁₂ absorption test was performed, it was found that both anemic and nonanemic worm carriers absorbed significantly less B₁₂ than controls. This pointed to the fact that D. latum, even in nonanemic carriers, impairs the absorption of vitamin B₁₂ by its host.

"The consequences of the latent B₁₂ deficiency of nonanemic worm carriers are not yet fully understood," he declared, "but it is worth mentioning that some of these patients develop neurological eye lesions."

Swimming Pools Store Water in Kenya Cholera Emergency

Medical Tribune World Service

NAIROBI—Kenyan officials have hit on a new way of fighting cholera—by using portable swimming pools as emergency water tanks.

When the recent cholera alert began, portable pools were flown from Nairobi to many outlying areas where the inhabitants normally rely on rivers and lakes for their drinking water. Water was pumped into the pools, treated to kill bacteria, and then drawn off again through a plastic pipe for drinking and washing.

Water-borne infection dropped sharply in areas where the emergency tanks were installed, officials reported.

Wednesday, September 22, 1971

MEDICAL TRIBUNE

Migraine Linked To Contraceptive In Some Women

Medical Tribune World Service

ELLSMORE, DENMARK—Oral contraceptives can bring out a latent tendency to migraine headache in some young women, and the correlation is even more marked when there was a previous history.

Clinical evidence of this, including a danger of thrombosis with permanent damage to the nervous system, was presented here by Dr. J. Desmond Carroll, consultant neurologist at the Regional Neurological Unit, Guilford, Surrey, England.

Dr. Carroll based his findings on studies made on two groups of women taking oral contraceptive pills. The first group consisted of 215 patients who had attended his clinic over a period of three years and who, prior to taking the pill, had never complained of significant headache. The second included 75 consecutive patients at the migraine clinic in whom there was a typical history of migraine headaches before leaving out the pill.

Two Headache Types Present

In all, 70 women (32 per cent) in the first group experienced headaches. These included 48 whose headaches were generalized and of a vague type and 22 (10 per cent) with lateralized headaches that were apparently of the vascular migraineous type.

"It is clear in this analysis," Dr. Carroll told an International Headache Symposium here held under the sponsorship of the American Association for the Study of Headache and the Danish Migraine Society, "that in 10 per cent of these patients the pill brought out an inherent susceptibility to migraine, but more often in those who had a family history of headaches or allergic disorders."

Despite the fact that many patients stopped taking the pill, this did not produce a complete remission of migraineous headaches in all cases.

Among the 75 patients in the second group, 37 reported a deterioration in their migraines that took the form of an increase in either frequency or severity or both.

A high proportion also noted a distinct change in the pattern of their attacks. In a few patients, focal symptoms accompanied the migraineous headaches for the first time.

Twenty-nine patients reported no change in the pattern of their migraine and nine reported a distinct improvement, especially in the degree of severity.

Opposite Results Reported

In the discussion following delivery of Dr. Carroll's paper, Dr. Par Olof Lundberg of Sweden pointed out that he had achieved opposite results to those of Dr. Carroll in a study on a larger, nonselected series.

Whereas Dr. Carroll's patients came from headache clinics, Dr. Lundberg's patients were taken from a contraceptive pill clinic.

Dr. Lundberg, who is Assistant Professor of Neurology at the University Hospital in Uppsala and president of the Swedish Migraine Society, encountered 228 women who had previously suffered from migraine among a total of 1,676 requesting prescriptions for the pill.

Following consumption of various oral contraceptives for a median period of one year, 66 of the women who had had had migraine suffered still worse from the affliction, but 129 of them experienced an improvement. This indicated an over-all favorable effect from the consumption of oral contraceptives.

Since the number of different drugs used in Dr. Lundberg's study was so great, it was impossible for him to determine which constituents had the most favorable effects.

However, he suspected that the high-progestogen pills were superior to the high-estrogen ones.

Armadillo May Provide Model For Investigation of Leprosy

Medical Tribune World Service

WASHINGTON—Research scientists at the U.S. Public Health Service Hospital, Carville, La., and the Gulf South Research Institute, New Iberia, La., have succeeded in transmitting lepromatous leprosy to an armadillo and believe that they have found a satisfactory animal model for investigation of the disease.

The work was reported at a press conference here by Dr. Waldemar F. Kirchheimer, chief of laboratory research at Carville, and co-workers, in cooperation with Dr. Eleanor E. Storrs, of the Gulf South Research Institute.

Dr. Jack Butler, PHS director of hospitals, described it as "a significant advance that could lead to control or eradication of leprosy."

An earlier technique for growing leprosy bacillus in the footpads of mice, he noted, is limited in its applicability by the fact that the infection does not spread beyond the site of the injection and the animal must be severely altered to mutilate the infection.

The Carville team succeeded in giving

leprosy to an armadillo injected with 18,000,000 live bacteria taken from a patient in Surinam. In February, 1970—a year after the injection—the armadillo manifested clinical signs of leprosy, developing large sores on both ear lobes, the injection site. Five months later the animal died—surprising the investigators, since the disease rarely kills human beings.

Tissue studies, Dr. Kirchheimer said, showed that the infection site contained about 20 billion bacteria for each gram—"five times as many bacteria as have ever been found in man." This suggests that the armadillo—or at least this particular animal—may be more susceptible to leprosy than man, he observed.

Investigators believe, Dr. Kirchheimer said, that armadillos will provide the long-sought acceptable animal model. They live long enough to get the disease, which in human beings may take three to five years to show clinical signs, he noted.

It has been noticed, he said, that only a few members of a particular animal species are susceptible to infection with bacteria resembling leprosy bacilli, and he therefore expects that an "as yet unknown



Leprosy has been transferred to a nine-banded armadillo, similar to one examined by Drs. Waldemar F. Kirchheimer (l.) and John Trautman, who is director of the USPHS Hospital, Carville, La.

proportion of experimentally infected armadillos will be susceptible and hence will develop the progressive form of the disease."

Dr. Kirchheimer speculated that the armadillo's unusual reproduction characteristics—it breeds easily and gives birth every time to a litter of four identical twins—might make it possible "to breed from a set of lepromatous parents fully susceptible armadillo populations."

1962 was a bad year for Staph infection

In a hospital study from 1960 to 1967, only 2 positive staphylococcal lesions were noted among 34,262 infants washed with pHisoHex®. Both occurred in 1962.

In 5 additional studies, 24 of 1974 infants washed with pHisoHex, Staph colonization was only 2.4%; while in 1160 "unwashed" control infants, colonization amounted to 45%.

Anti-Staph protection for the infant usually begins with a pHisoHex bath before he leaves the delivery room. It can be continued and strengthened throughout the infant's stay in the hospital nursery by bathing him daily with pHisoHex and having everyone who handles the infant wash his hands with pHisoHex before and after handling the baby. This routine builds a cumulative, disease-resistant film of antibacterial hexachlorophene on the skin to form a powerful barrier against Staph and many other bacteria.

Mother can maintain this antibacterial protection at home by bathing baby exclusively with pHisoHex. And nonalkaline, hypoallergenic pHisoHex is kind to skin. Won't dry or tend to irritate even when used frequently.

References: 1. Gluck, Louis: *Hosp. Practice* 3:33, Jan. 1968 (author's correction). 2. Payne, Margaret C.; Wood, H. F.; Karakawa, Walter, and Gluck, Louis: *Am. J. Epidemiol.* 82:305, Nov. 1965. 3. Gluck, Louis, and Wood, H. F.: *New England J. Med.* 285:1177, Dec. 14, 1961. 4. Simon, H. J.; Allwood-Poretsky, Juan, and Treloar, Attona: *Pediatrics* 36:254, Feb. 1965. 5. Gluck, Louis, and Wood, H. F.: *New England J. Med.* 285:1285, June 8, 1968. 6. Simon, H. J.; Yatta, G. J., and Gluck, Louis: *New England J. Med.* 285:1171, Oct. 14, 1961.

Winthrop Laboratories, New York, N.Y. 10016



pHisoHex
antibacterial skin cleanser with 6% hexachlorophene

NEWS INDEX

Diagnosis

Automated instrument proves accurate in detecting pre-eclampsia1

Immunization

Condehill vaccine preferred against rubella in women of childbearing age1

Radiology

Liver scan's lack of specificity in cancer patients is stressed1

Medical Groups

Hospital association votes to endorse Nixon's wage-price freeze1

CLINICAL NEWS NOTE: "Clinical experience has shown that intravenous magnesium sulfate is frequently efficacious in treatment of abrupt onset of convulsions in patients undergoing fluid therapy for cholera." (Dr. Akio Kobayashi, specialist in nephrology and gastroenterology at the National Children's Hospital, Tokyo; see above.)

Ob/Gyn

Oral contraceptives may induce migraines in some young women3

Research (3,16)

Armadillo is found to be satisfactory model for study of leprosy3

Pharmacology

HEW devising test to assess efficacy of drugs used for depression5

Congenital Diseases

Evidence supports need for early treatment of hypothyroidism17

Neurologic Diseases

Amantadine hydrochloride is said to relieve parkinsonian symptoms18

Pediatrics

British M.D. provides guide for informing parents of handicapped child18

FEATURE INDEX

In Consultation5
Chess Problem9
Cartoons9,11,16
Editorials11
Letters to Tribune11
Epigram14
Medicological Report21
Medical Meeting Schedule21
Sports Report23
Immateria Media23
Coming next issue: see page 5

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happy anniversary?



A time for her to look back. For you to look ahead... to the long course of therapy required to hold her blood pressure down.

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Ismelin[®] sulfate (guanethidine sulfate) the antihypertensive for what may lie ahead

INDICATIONS: Primarily for severe or sustained elevation of blood pressure (particularly diastolic) and almost all forms of fixed and progressive hypertensive disease, even when blood pressure elevation is moderate. Not recommended for labile or milder forms of hypertension.

CONTRAINDICATIONS: Proven or suspected pheochromocytoma; hypersensitivity to Ismelin. Do not use with MAO inhibitors.

WARNINGS: Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Warn patients not to deviate from instructions and about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during initial dosage adjustment and with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking Ismelin. Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer pressor agents and anesthetic agents cautiously in reduced dosage with oxygen, atropine, and vasopressors ready for immediate use. Give vasopressors with extreme caution because patients on Ismelin may have a greater propensity for cardiac arrhythmias. Febrile illness may reduce dosage requirements. In frank congestive heart failure not due to hypertension, Ismelin is not recommended. Due to catecholamine depletion and increased responsiveness to norepinephrine, special care is required when treating patients with a history of bronchial asthma, since the condition may be aggravated.

Use in Pregnancy

The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

PRECAUTIONS: Give very cautiously to hypertensives with (a) renal disease with nitrogen retention; (b) coronary disease with insufficiency or recent myocardial infarction; (c) cerebral vascular disease, especially with encephalopathy; and (d) rising BUN levels. Give with extreme caution to those with severe congestive failure. Watch for weight gain or edema in patients with incipient cardiac decompensation. If digitalis is used with Ismelin, remember that both drugs slow the heart rate.

Appetite suppressants (eg, amphetamines), mild stimulants (eg, ephedrine, methamphetamine), and tricyclic antidepressants (eg, imipramine, nortriptyline, doxepin) may decrease the hypotensive effect of Ismelin. Wait one week after discontinuing MAO inhibitors before starting Ismelin.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver function tests are advised during prolonged therapy.

ADVERSE REACTIONS: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. Less frequently—dyspepsia, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, pruritus of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (angina), chest paresthesias, nasal congestion, weight gain, and asthma in susceptible individuals.

DOSAGE: Initial dosage should be low and increased gradually by small increments.

Before starting therapy, consult complete product literature.
HOW SUPPLIED: Tablets, 10 mg (pale yellow, scored) and 25 mg (white, scored); bottles of 100 and 1000.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

C I B A

Wednesday, September 22, 1971

MEDICAL TRIBUNE

The Consultant

DR. SAMUEL J. FOMON
Professor of Pediatrics, the University of Iowa University Hospitals, Iowa City.

What's new and important in the field of infant nutrition?

IMPROVEMENTS IN THE HEALTH CARE of infants in at least the major segment of the U.S. population have meant that many physicians are no longer fully occupied with emergency management of life-threatening diseases such as whooping cough and diarrhea. It has therefore become feasible to turn our attention to possible later consequences of feeding during infancy.

The questions now being formulated are enormously complex, and it would be unrealistic to anticipate that they will be satisfactorily answered within the next two or three years. Does intrauterine growth retardation influence the infant's potential for physical and mental growth? Do feeding practices in infancy contribute to the problems of obesity and atherosclerosis in the adult population? How should we define obesity in infancy? What is a physiologically sound definition of iron-deficiency anemia? I believe that these and similar questions represent the future course of research in infant nutrition in technologically advanced societies.

In the past few years, however, we have become acutely aware of the existence of other, more immediate problems. With much of the U.S. population well-nourished and, in fact, quite many of them overfed, a minority of the population nevertheless appears to be suffering from various types of malnutrition. We need to determine the size of this group and to devise means of assuring adequate intakes of calories and individual nutrients.

What is your attitude toward breast feeding?

My bias leads me to believe that any breast feeding is better than no breast

feeding—providing that the mother finds this method of feeding attractive. I do not believe that women in technologically advanced societies should be coerced into breast feeding. Until evidence to the contrary is presented, I am inclined to evaluate performance of formula-fed infants on the basis of performance of breast-fed infants. However, only about 27 per cent of U.S. infants are breast-fed for even a few days, and only about 15 per cent for as long as two months.

Our studies indicate that breast-fed infants gain in weight and length less rapidly than do formula-fed infants. We suspect on this basis that formula-fed infants may be overfed. When a breast-fed infant ceases to suck and swallow, his mother will assume that he is satisfied. Happily, she does not know how much he has taken. The formula-fed infant, on the other hand, is commonly encouraged to drain the bottle.

Which infant feeding practices are likely to have later consequences?

One I have already mentioned is overfeeding. Various investigators have speculated that overfeeding during infancy results in formation of an excessive number of fat cells. It is possible, however, that the number of fat cells might be normal during infancy but that habits of overeating, carried over to adult life, would eventually be responsible for an increase in number and/or size of fat cells.

Another possibility is that an excessive intake of sodium during infancy may predispose to hypertension. High intakes of sodium might induce hypertension directly—as has been demonstrated with rats of certain hypertension-prone strains. Or,

Chemical Test for Antidepressives To Be Evaluated by Units of HEW

Medical Tribune Report
ROCKVILLE, Mo.—A study to evaluate a simple chemical test for assessing the potential efficacy of certain drugs proposed in the treatment of depression has been announced by HEW's National Institute of Mental Health and Health Services and Mental Health Administration.

The study focuses on monitoring the pharmacologic activity of the tricyclic drugs commonly used in treating depression. These include imipramine, amitriptyline, and others.

The project director is Dr. Seymour Rosenblatt, of the Mount Sinai School of Medicine, New York. He says that a better understanding of the pharmacologic activity of these tricyclic antidepressants

could lead to furthering "our understanding of some of the biochemical aspects of depression." Therapists estimate that between 4,000,000 and 8,000,000 Americans are in need of professional care for a depressive illness at any given point in time.

The test being studied consists of administering a small tracer dose of norepinephrine and determining the relative distribution of nonoxidized amine (N) and oxidized (O) metabolites (N/O ratio) in a urine specimen 12 to 20 hours later.

Considered relatively simple, this test has been confined largely to research use, but according to Dr. Rosenblatt it is easier and provides more precise data than the blood tests now used.

Previous research has implicated norepinephrine as a possible factor in depression. The illness has been associated with a deficiency of the transmitter hormone in the central nervous system. The tricyclic drugs may be effective against depression because they somehow correct an error in central nervous system functioning that too rapidly depletes the available supply of norepinephrine.

Specifically, Dr. Rosenblatt will study to what extent the N/O ratio in urine correlates with patient improvement, whether or not pretreatment N/O ratios may indicate if a patient will do better on other than a tricyclic drug, and whether or not the ratios will allow an early evaluation in the patient's treatment of the efficacy of a particular tricyclic drug.

Next Tribune Consultant

DR. JOSEPH I. GOTTSMAN, Professor and Chairman, Department of Otolaryngology, Mount Sinai School of Medicine, New York.



...and some questions he will answer:

- Comment on the problem of auditory nerve deafness secondary to antibiotic therapy.
- Does any indication exist currently for the early operation of fenestration for otosclerosis?
- What are the indications for radiotherapy and for surgery in tumors of the larynx?

provision of a daily intake of iron-fortified foods or of medicinal iron.

The iron content of unfortified foods is too low to permit achievement of recommended intakes except in the most unusual instances. Iron-fortified infant foods consist of formulas and of infant cereals. Several manufacturers have indicated that well over half of their sales of formulas consist of the products that are not fortified with iron—even though the same formula fortified with iron is marketed at the same price.

Iron-fortified formulas are well tolerated by infants, and I fully agree with the Committee on Nutrition that infants fed commercially prepared formulas should receive the iron-fortified products. Because iron can also be provided in infant cereals or in medicinal iron, I see no need to encourage feeding of iron-fortified formulas until age one year.

The most often
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Check the price to
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When analgesia is needed for a long period

■ Comparable to codeine in analgesic efficacy: one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine.

■ Prolonged analgesia between doses: relieves pain usually for 3 hours or longer. Onset of significant analgesia usually occurs within 15 to 30 minutes.

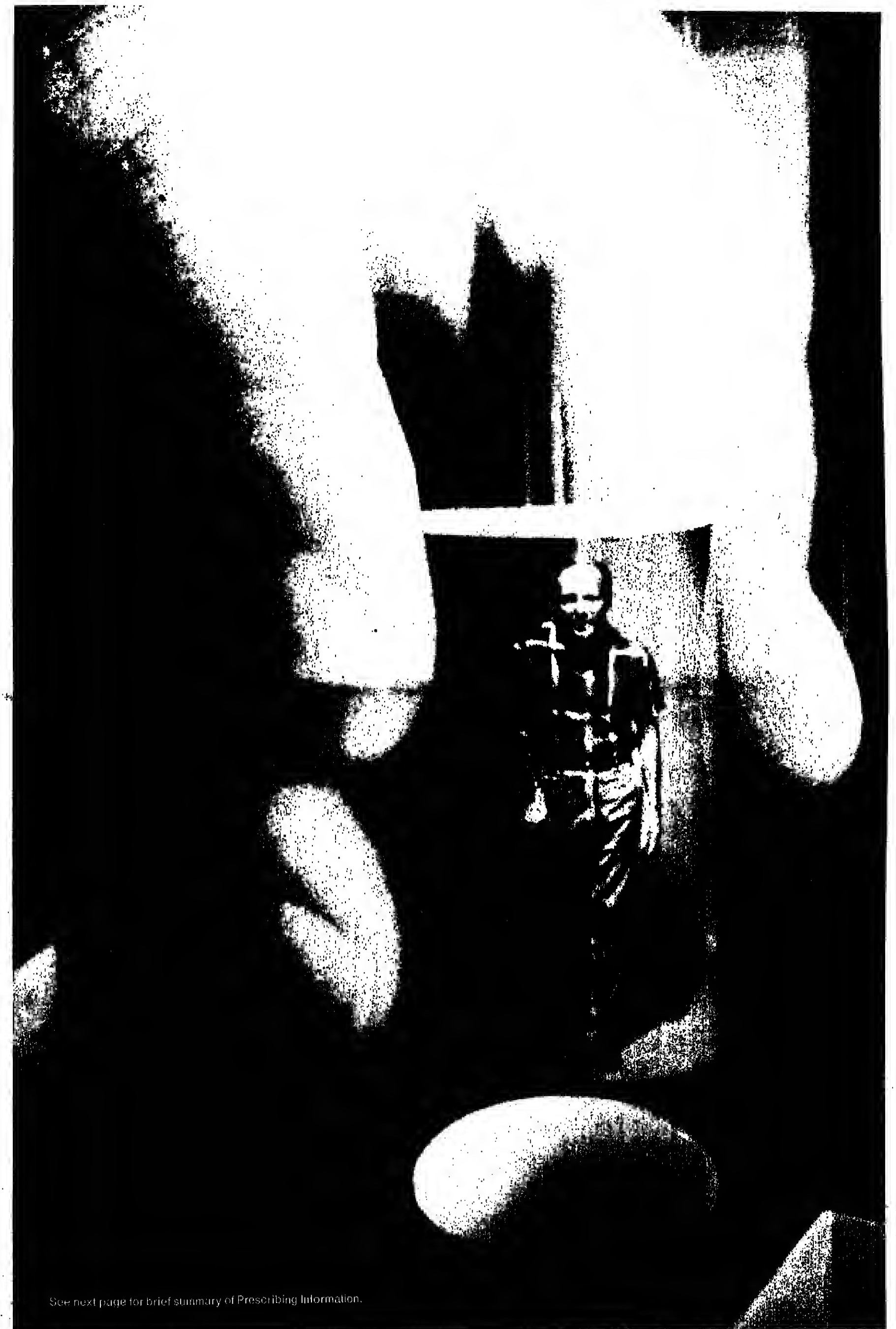
■ Tolerance to the analgesic effect of Talwin Tablets has not been observed and no significant changes in clinical laboratory parameters attributable to the drug have been reported.

■ Infrequently causes decrease in blood pressure or tachycardia; rarely causes respiratory depression or urinary retention; seldom causes diarrhea or constipation.

■ Generally well tolerated by most patients: if dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See Product Information following for full discussion of all adverse reactions and other prescribing information.)

■ Not subject to narcotic controls; convenient to prescribe—day or night.

A time for Talwin[®] brand of pentazocine (as hydrochloride) 50mg. Tablets



See next page for brief summary of Prescribing Information.

moderate to severe pain

A time for Talwin®

brand of
pentazocine 50mg. Tablets
(as hydrochloride)

Contraindications: Talwin should not be administered to patients who are hypersensitive to it. **Warnings:** Head Injury and Increased Intracranial Pressure. The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain. **Acute CNS Manifestations.** Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: Cardiac Respiratory Conditions. Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma, and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accumulation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.



Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effects. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include gastroenteric: nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea.

CNS effects: dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see Acute CNS Manifestations under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. **Autonomic:** sweating; infrequently flushing; and rarely chills. **Allergic:** infrequently rash; and rarely urticaria. **Cardiovascular:** infrequently decrease in blood pressure, tachycardia. **Other:** rarely respiratory depression, urinary retention.

Dosage and Administration: Adults. The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin. **Children Under 12 Years of Age.** Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

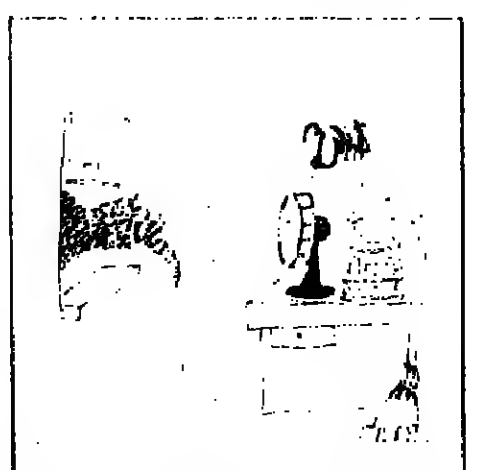
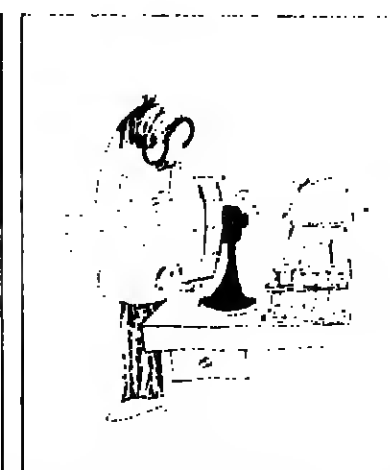
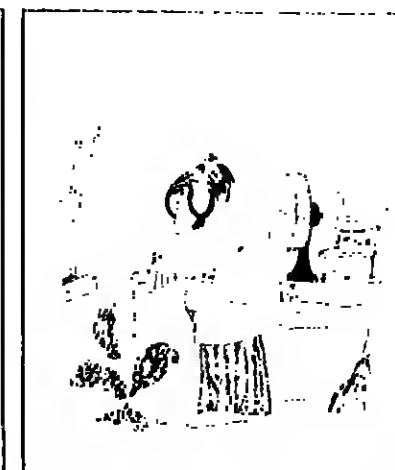
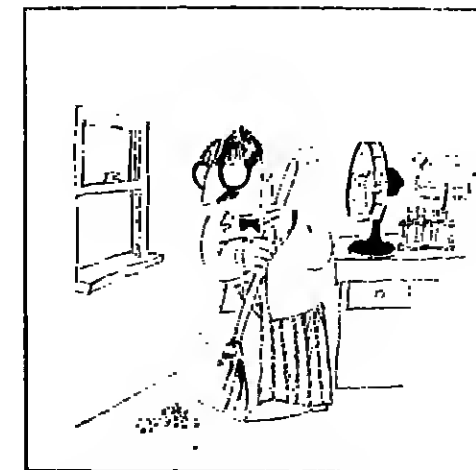
Overdose: Manifestations. Clinical experience with Talwin overdose has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are not effective antidotes for respiratory depression due to overdose or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the anesthetic, methylnalphenate (Ritalin®), may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls. **How Supplied:** Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

Winthrop Winthrop Laboratories, New York, N.Y. 10018

Clinical Trials



Cendehill Rubella Vaccine Held Most Suitable in Fertile Age

Continued from page 1

Jamaica 46 per cent of females in the childbearing age are seronegative, and in Hawaii susceptibility in adult men and women has varied from 25 to 50 per cent.

"The pockets of unusually high rubella susceptibility among women in the childbearing age groups naturally represent special problems to the health authorities in those areas," Dr. Gold said. "Some—and I believe rightly so—have undertaken selective rubella vaccination of susceptible adolescents and young adult girls."

Dr. Gold noted that clinical trials of rubella vaccine on mature women in the United States and Europe have been in most cases limited to the Cendehill vaccine. Experiments carried out on approximately 800 susceptible women have shown a seroconversion rate ranging between 97 and 100 per cent and an incidence of joint reaction, usually mild arthralgia, of 6 per cent.

In studies conducted by Dr. Gold's group, the incidence of arthralgia in 115 susceptible female subjects who received Cendehill vaccine was 7.8 per cent, compared with 4.7 per cent in seronegative placebo-inoculated women. The incidence of arthritis was even lower—1.7 per cent in seronegatives receiving vaccine and 0.9 per cent in the seronegative placebo group.

10% of Joint Manifestations

The incidence of joint manifestations associated with the administration of Cendehill vaccine is approximately 10 per cent; with HPV duck embryo vaccine it is 38.5 per cent and with HPV 77 dog kidney vaccine 48 per cent.

A postpartum comparison study has reported essentially the same reaction rate for Cendehill and HPV 77 vaccines, but joint swelling, limitation of motion, and pain of longer duration were found with greater frequency in susceptible HPV recipients.

Commenting on postpartum studies in the United States, he reported that approximately 400 women have been vaccinated and seroconversion rate was 95 per cent.

Hormonal or other physiologic changes

that occur during the postpartum period do not produce undesirable side effects and do not interfere with the rubella antibody response.

Dr. Gold said he was aware of approximately 38 cases of clinically normal children born to women who received rubella vaccine shortly before or during early pregnancy.

The infants had a negative virus work-

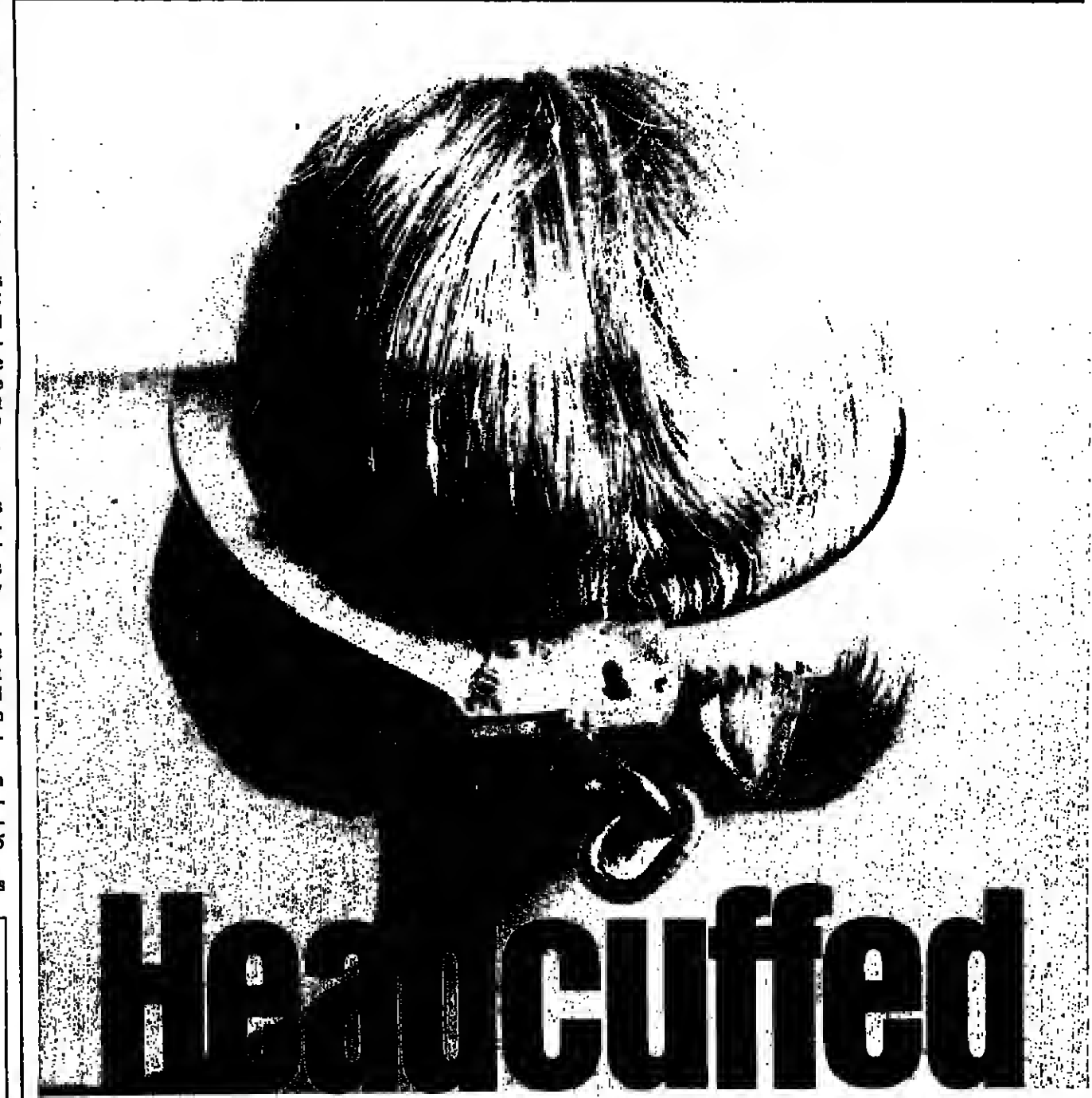
up, and their sera were negative for IgM.

He noted that the risk to pregnant women is much lower from vaccine virus than from the wild strain and added there is a possibility there may be a difference in risk among the different vaccines.

All antibody in children and adult women following Cendehill vaccination is found quite early. Of those tested by Dr.

Gold's group, 96 per cent of those tested between the 20th and 24th days seroconverted, as did 97 per cent of those tested between the 25th and 29th days.

Early seroconversion after vaccination has also been noted with HPV 77 dog kidney vaccine, but HPV 77 duck embryo vaccine appears to produce some delay in detectable antibody. Only 78 per cent of 49 susceptible women developed antibodies by the 28th day of a recent series of tests, Dr. Gold said, although all had antibody by the 56th day.

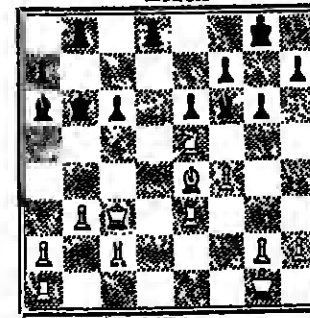


Headcuffed

by tension headache

Chess Problem

Black



White

This position arose in a game between the Soviet masters Kaminiski and Osnos. White has just played P-QN3 and seems safe enough despite two separate pins to combat. How did Black continue? See page 17.

Let Fiorinal help release the patient from the aching, pressing, painfully tight feeling of tension headache. Its analgesic components help relieve pain while its sedative component helps relax the patient.

SANDOZ PHARMACEUTICALS
EAST HANOVER, N.J.



ANALGESIC plus SEDATIVE®

Fiorinal®

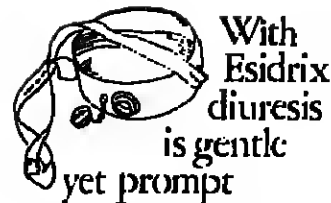
Each tablet or capsule contains: Sandoptal® (butalbital) (Warning: May be habit forming) 50 mg.; caffeine, U.S.P., 40 mg.; aspirin, U.S.P., 200 mg.; phenacetin, U.S.P., 130 mg.

Contraindications: Hypersensitivity to any of the components.

Precautions: Due to presence of a barbiturate, may be habit forming. Excessive or prolonged use should be avoided.

Side Effects: In rare instances, drowsiness, nausea, constipation, dizziness, and skin rash may occur. **Adult Dosage:** One to two tablets or capsules, repeated if necessary up to 6 per day, or as directed by physician. **Before prescribing, see package insert for full product information.**

Avoid the complications of "diuretic overdry"



No one denies there's a time and place for a highly potent nonthiazide.

But most patients rarely need it. Which is why hydrochlorothiazide—originated by

CIBA as Esidrix—remains the most widely used oral diuretic.

With Esidrix you usually avoid the abrupt flushing out common with fast-acting nonthiazides.

Diuresis is prompt; edema is relieved gradually over a 12-hour period. Which is usually fast enough. Just as important, it's smooth and gentle.

Moreover, the risk of serious salt and water loss is reduced.

However, since fluid and electrolyte imbalance may occur, patients should be watched closely for clinical signs (please see brief prescribing information).

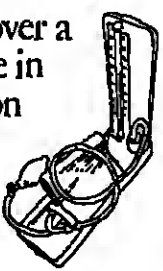
Things are complicated enough for the edema patient. Rely on Esidrix, the smooth, gentle diuretic. Particularly in maintenance therapy.

Proven by over a decade's use in hypertension

Esidrix is still unsurpassed as a diuretic-antihypertensive. Labeling for one newer nonthiazide states: "Hypertensive patients who cannot be adequately controlled with

thiazides will probably also not be adequately controllable with [furosemide] alone."

And Esidrix is amply proven alone in mild hypertension. As an adjunct in mild to severe cases.



Esidrix
(hydrochlorothiazide)
is often just enough



Dorothy Lamour—star of stage, screen and television.

Esidrix® (hydrochlorothiazide)

Indications: Edema and hypertension. Contraindications: Anuria; disordered renal function. Dosage should always be carefully titrated.

Pay special attention to electrolyte balance of patients with severe hepatic insufficiency. In patients with cirrhosis and ascites, watch for symptoms of impending hepatic coma (confusion, drowsiness, tremor) and for increased arterial ammonia concentration. Sodium and potassium excretion. Thiazides may decrease glucose tolerance; use cautiously in diabetics. Hypokalemia may occur but is generally reversed by a uricosuric agent.

Thiazides may decrease arterial responsiveness to norepinephrine and increase responsiveness to norepinephrine; if possible, withdraw therapy 2 weeks prior to surgery. Hypotensive episodes under anesthesia have been observed. If emergency surgery is indicated, preanesthetic and anesthetic agents should be administered in reduced doses.

The possibility of sensitivity reactions should be considered to patients with a history of allergy or bronchial asthma.

Use in Pregnancy: Thiazides should be used with caution in pregnant or lactating patients since this drug crosses the placental barrier and appears in breast milk and may result in fetal hyperbilirubinemia, thrombocytopenia, or altered carbohydrate metabolism. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

Precautions: Perform serum potassium, BUN, uric acid, and blood sugar tests prior to and at appropriate intervals during therapy. Watch patients for clinical signs of fluid or electrolyte imbalance (hypokalemia, hypochloremic alkalosis, hypokalemia). Warning signs: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, GI disturbance. Signs and urine electrolyte determinations are particularly useful in detecting renal impairment, discontinue drug if oliguria, retention indicates onset of renal impairment, discontinue drug.

Adverse Reactions: Gastrointestinal—nausea, gastric irritation, anorexia, vomiting, constipation, diarrhea, cholestatic jaundice (intrahepatic cholestasis), pancreatitis, hyperglycemia, glycosuria. Central nervous system—dizziness, vertigo, parosmia, headache, syncope, ataxia, depression, confusion, photophobia, rash, urticaria, necrotic angitis. Hematologic—leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Miscellaneous—muscle spasm, weakness, restlessness. When severe reactions are moderate or severe, reduce dosage or withdraw therapy.

Consult complete literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07961

CIBA

The Only Independent Medical Newspaper in the U.S.

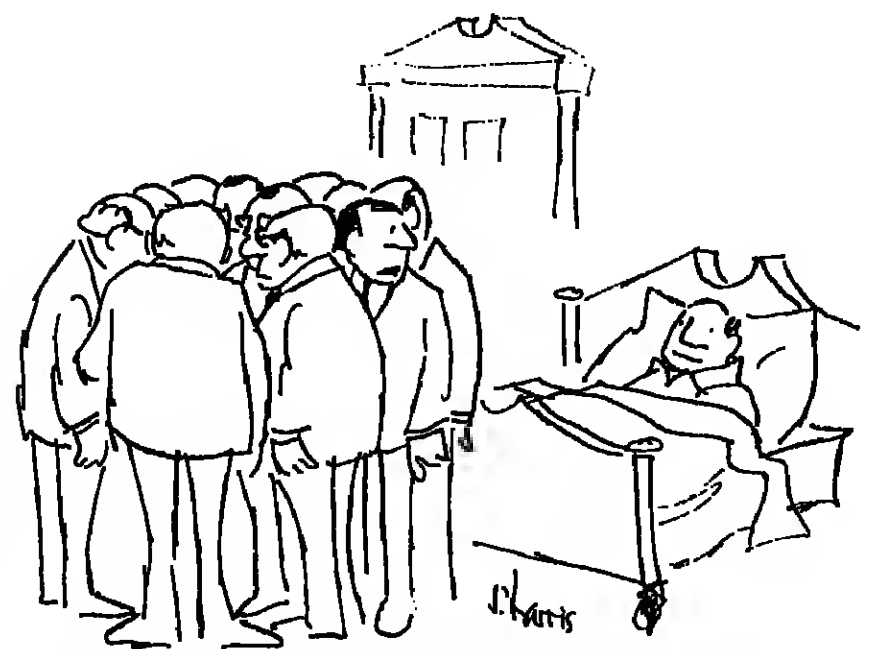
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"But why on earth, Mr. Fobbar, would you want an 11th opinion?"

On the Free Press

THE HYPOTHESE of the Bill of Rights, as noted by Senator Ervin of North Carolina, is the First Amendment. That amendment guarantees "Congress shall make no law . . . abridging freedom of speech, or of the press." In the 18th century, speech went as far as the voice could be carried by sound waves but the press included newspapers, books, fliers, bills, and other documents. Today the means of communication are broader and extend to mass media, such as radio and television, and to specialty publications of far more limited distribution, such as MEDICAL TRIBUNE.

In espousing the freedom of communication, our First Amendment makes no distinction among media nor does it make any reference to the media's financial structure. In effect, it is an amendment that secures freedom of communication, and, as recent events have shown, that freedom of communication is sacrosanct also for radio and television; it must extend, as well, to all arms of the press, including controlled (free) circulation publications whose financial viability depends on advertising. At this time, it turns out, the dependence on advertising for viability is not limited to controlled circulation publications alone.

In a recent article on the editorial page of the *Washington Post*, Richard Harwood reported that the *Post's* subscription and newsstand income last year amounted to no more than \$13,000,000, while its total income was \$77,000,000, with a profit of \$9,000,000. The cost of the blank paper alone on which the newspaper was printed came to \$20,000,000—greater by more than a half than all the subscription and newsstand income. Said Mr. Harwood, "It was the advertisers who kept us alive and prosperous; they spent \$64,000,000 for space in the *Washington Post* last year. Without their dollars we could not survive in our present form and that is true of every daily newspaper in America." The distinction between free circulation media—and that includes television and radio (also part of the *Washington Post* communications complex) as well as con-

trolled-circulation newspapers—and the so-called subscription publications is neither real nor even academic.

Those who insist that advertisers "call the tune to which the American press dances" and that our media are controlled by vested interests must acknowledge that there are a host of others with "axes to grind." There are professional bodies, public figures, and even individual scientists and physicians who, by reason of personal conviction or, sometimes, for personal prestige, seek wide dissemination of their views and opinions, whether generally accepted ones or highly controversial. There are reporters, whose advancement may seem to rest on the ability to produce exciting coverage; columnists, whose syndication and financial reward may be increased by sensationalism; even editors, necessarily interested in circulation figures that may be altered by the manner in which news is handled. In the light of these disparate interests, how can our organs of communication remain truly free? That is possible only when freedom is linked with responsibility.

MEDICAL TRIBUNE, as a unit of the medical press, has from the first day of publication refused tobacco and liquor advertising; this was done voluntarily, simply out of a sense of medical responsibility. On the other hand, other publications that frequently attack the medical press see no inconsistency in carrying such attacks sandwiched between pages of cigarette and alcohol advertising. We trust that a recognition of the responsibility of the press will lead the print media to a voluntary assumption of the course of action now legislatively imposed on radio and television in regard to cigarette advertising.

The question of what advertisements a newspaper carries, however, is secondary to the integrity of its news columns and editorials. It is our belief that, as in the practice of medicine, the integrity of the American press is best assured by the ethics and principles of professionals—the ethics and principles of reporters, of columnists, of editors, and of publishers.

Underwater Swimming and Hypoxia

CLINICAL QUOTE: "Loss of consciousness during underwater swimming can occur when the swimmer is trying to set a record for distance and time. Invariably, the subject voluntarily hyperventilates before the swim. Loss of consciousness occurs with little or no warning, and the subject may continue to swim for a time despite such loss. People watching often do not realize that the swimmer is in trouble until final collapse. Death is a common re-

sult. The breaking point signal occurs even if he is exercising. . . . When exercise is combined with the breath hold following hyperventilation, the partial pressure of oxygen decreases even faster and hypoxia is quite easy to produce. . . . and occurs with little or no warning." (Dr. Albert B. Craig, Jr., Associate Professor of Physiology at the University of Rochester School of Medicine and Dentistry; see *Sports Report*, page 23.)

National Health Insurance

Editor, MEDICAL TRIBUNE:

I have two comments on your edition of March 17 necessary for clarification of editorial and bureaucratic welfare state thoughts expressed therein.

The first is directed to your presumption that national health insurance is the only prospect for future medical practice. To this cliché, if enough physicians take the trouble to study the results of socialized medicine in other countries, their vociferous answer would be "No." In that case the "inside" promulgators of this inferior type of medical care would be stopped by a lack of physician participation, and taxpayers would be spared another federal boondoggle.

The second comment is directed to the Nixon health message that would fritter away more taxpayers' money on HMOs, subsidized health insurance, a stacked malpractice insurance commission, and further subsidized medical students and colleges. All of these suggestions are but variations of the Altmeyer, Cohen, Falk efforts to socialize medicine for the past years and are in total violation of the oath of office pledged by Nixon.

Since your editorial implies acceptance of bureaucratic buncombe for the practice of medicine, I suggest that you review the effects of Federal interference in the areas of farming, labor, housing, welfare, communications, and transportation. We are now paying for those mistakes, and many more, to the tune of more debt than all the rest of the nations in the world.

A. G. BLAZBY, M.D.
Washington, Ind.

Sex in Schools

Editor, MEDICAL TRIBUNE:

Direct experience with sex education programs reveals that sex courses provide the same type of information that overwhelms the child from the pornographic media. Because teachers act as parent substitutes, what the student learns is usually accepted as correct sexual information. The Anna material presented in under-the-counter magazines is frequently regarded as fantasy. Consequently, the results from schooling are more serious.

School teachers presiding over coeducation sex classes cannot correctly develop a child's sexuality. Indoctrination with sexual knowledge . . . is by no means a prerequisite for a normal sexual development affording an appreciation for *nature's* heterosexuality. Nor is knowing about intercourse and genital anatomy a means of preventing sexual maladjustments. Similarly, textbook sex information is not needed for a child's sexual maturation

and, in fact, interferes with natural responses to childhood sensual impulses.

Only parents or those responsible for a child's total care can, in reality, influence the child's latent sexual instinct and sexual growth. Through child-parent relationships the young person learns that physical love is inseparably entwined with affectionate love. By example the mother and father show that sex is a one woman-one man affair. . . . Civilized societies derived from family life are entirely dependent on maintaining the intimate nature of sex. Only in a horde culture can sex be accepted as an entirely open matter, freely exposed.

Group participations in sensual sex, whether by means of actual sex acts, through the use of the pornographic media, or with the help of classroom programs, are contrary to the normal intimate nature of sexuality. Anyone responsible for teaching people how to have intercourse should be aware of this intimacy. However, sex educators seem to ignore the unnaturalness of learning about sexual experiences in the schoolroom. In this attitude they are bolstered by some modern-day psychiatrists, who have been trained in the peculiar setting we call the psychiatric hospital. These teachers and psychiatrists proclaim intimacy is not an integral part of the sex instinct. They say intimate feelings are reflections of "hang-ups" due to the rigidity of society's established codes.

To substantiate their view, they often cite the "scientific" studies of university sex professors. The published words of these academicians, devoid of any real medical experience, are derived from their note jottings taken while they watch male and female "volunteers" perform sex acts (Masters and Johnson, *Human Sexual Response*). From such data the sex scientists deduce, for their worshippers of scholasticism, what sex is all about. However, observations obtained from everyday clinical practice and judgments based on reason and personal introspection attest to the truth of Freud's teaching that intimacy is an inborn part of human sexuality. (Standard Edition of Complete Psychological Works of Sigmund Freud, Hogarth Press) . . .

Because I have testified as an expert witness in court cases involving libertine sex programs, I have had an opportunity to examine a significant number of sex curricula used in public schools. I find that though the courses make no pretense of teaching morality, invariably family values based on Judeo-Christian ethics are undermined and students are encouraged to set up their own standards devoid of sexual sublimations. . . .

MELVIN ANCHELL, M.D.
Los Angeles, Calif.



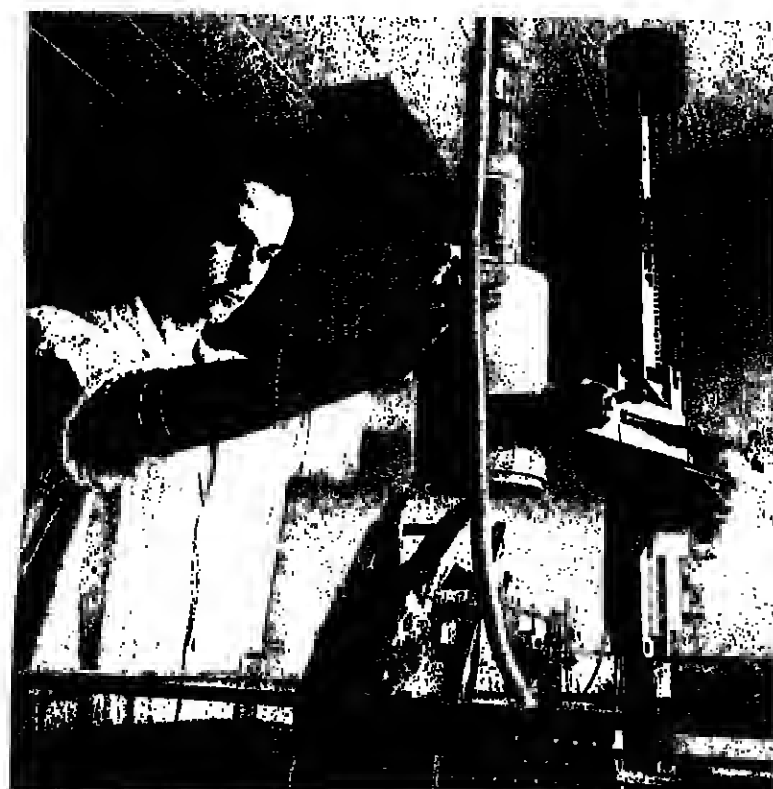
Necker staff is briefed by Dr. Jean Hamburger. In 1962 he performed first successful kidney transplant between nontwins.



Rat receives kidney transplant. Work

Paris Center Treats and Studies Kidney Disease

Its Three Units Have Total of 76 Beds



Renal blood flow in rabbit is measured, using radioactive gas method.

ADVANCED MEDICAL CARE, research, and training facilities are brought together at the Hôpital Necker, in Paris, to focus on the problems in the treatment and study of kidney disease.

The constant cross-exchange between applied and basic researchers have resulted in numerous innovations, including a presterilized, disposable artificial kidney and the technique of cytondherence, a highly sensitive test for checking donor compatibility.

The patients in Necker's three units, which total 76 beds, receive benefits of latest facilities. Special patients stay in a regulated antiseptic environment and communicate with visitors only via an intercom. Approximately one-fifth of Necker's patients participate in the home dialysis program, whose goal is to allow them to lead as normal a life as possible.

Many physicians from France and other countries attend the regular seminars and conferences or obtain fellowships for study at the center.



Patient is aided by staff in two-month training treatments, which is



Personality and Coronary Heart Disease

Although coronary heart disease (CHD) is the leading cause of death in the United States, its pathogenesis remains a complex, multifactorial puzzle. Certain physical factors have long been suspected. But, on the basis of recent prospective investigations, the impact of environmental stress on certain personality types may turn out to be as crucial as the presumed physical causes of CHD.

The following discussion presents some of the clinically significant findings that have emerged from recent extensive studies on this aspect of the problem.

A consensus, however, awaits the outcome of further definitive work.



Assay: Specificity of detection test for cancer of the rectum and colon, developed by Canadian Dr. Phil Gold, that measures carcinoembryonic antigen levels in the blood, is being evaluated by Tufts-New England Medical Center researchers under a new National Cancer Institute grant. Above, Drs. Robert Schwartz (c.), James Patterson (r.) and Larry Nathanson.



A Taste of Medicine: Medical students, Houston, have piloted a 10-week work-study program for high school grads. It was designed to give them a taste of lab work and aid in preparing them for college requirements. Above, Carla Whittaker (l.)

Interplay of endogenous behavioral traits and exogenous pressures

Rosenman and his associates^{2,3} have done a prospective study involving more than 3500 subjects at risk for occurrence of coronary heart disease. Their findings suggest that exhibition of a specific, overt behavior pattern (superimposed on additional prognostic risks such as hypertension and/or abnormal lipoprotein pattern) "...may bear a dominant pathogenetic relevance to the increasing coronary morbidity of the middle-aged American male." According to these clinicians, a distinctive pattern of recognizable personality traits can usually be found in the individual who ultimately incurs the disease. The subjects of their study exhibited two dissimilar types of personality and behavior: Pattern Type A and Pattern Type B.

Pattern Type A is characterized by "...excessive drive, aggressiveness, and ambition, frequently in association with a relatively

greater preoccupation with competitive activity, vocational deadlines, and similar pressures."³ Subjects in this group usually exhibit an enhanced sense of time urgency. Pattern Type A tends to speak frequently, rapidly, explosively. They are given to sudden gestures such as fist-clenching, desk-pounding, tant facial grimaces. Their movements are generally rapid, reflecting chronic restlessness, impatience and urgency.² Pattern Type B, on the other hand, is characterized by a relative absence of the emotional interplay and personality described for Pattern Type A.³

The results of the study by Rosenman and his associates demonstrated a significantly higher incidence of new coronary heart disease in the group designated as Type A. The authors emphasize, however, that occlusive CHD probably results from a complex interaction of many factors; that it was only when the Type A behavior pattern occurred in association with other prognostic factors such as elevated diastolic pressure or serum lipids or both, that the personality pattern had prognostic significance. For Pattern

Type B, on the other hand, even when the other prognostic risks were present, the incidence of new CHD was no greater than that observed for the total subject population at risk. These findings appear to have prognostic relevance.³

Concerning the stressful effects of a sense of time urgency, Pepitone⁴ has observed: "The existence of a deadline is commonly identified as a source of stress." He notes a report of some years ago "that tax accountants have high levels of serum cholesterol and thrombin as the deadline approaches for filing returns."

An "ideal" coronary candidate?

An attempt to identify the "ideal" candidate for heart disease in terms of a general stress model was outlined in a recent workshop on social stress and cardiovascular disease.⁵ "The ideal candidate...would be an individual who has been subjected to many stressful events, internal or external, which

have high valence for him; who is anxious and does not overtly express his aggression or frustration; who has to mobilize a great amount of effort to handle these stressful events or who feels that he is helpless to do anything about them."

Smoking and CHD: anxiety a common denominator

Thomas⁶ has recently called attention to an observed relationship involving anxiety, cigarette smoking and coronary disease. She points out that this is not necessarily a simple cause-and-effect relationship, but possibly could be explained on the ground that cigarette smokers are more often the precoronary type than nonsmokers.

Is there more than one "coronary personality" type?

Certain recent studies^{7,8} have suggested that there may be more than one major coronary personality type with differing be-

havioral patterns. In one study, exploring differences between coronary and noncoronary patients, it was found that the coronary group contained two subgroups, one that was described as self-centered, unstable, passive-regressive, mother-oriented—with coronary attacks occurring early in life—and the other almost opposite in character, described as sociocentric, controlled, striving, father-oriented—with coronary attacks occurring relatively late in life. The former group was generally low in ego strength whereas the latter showed considerable ego strength. The mother-oriented group demonstrated a high level of anxiety in connection with their "dependent self-image and life situation." Both groups, however, "had failed to establish their own identities in a satisfactory manner."

In discussing the prospective study of Rosenman and his group,³ which strongly related Type A behavior to CHD, Thomas⁶ notes that a substantial number of Type B subjects "...did develop coronary disease..." though less than those with Type A behavior pattern.

In a critique of studies on the current concepts of the "coronary-prone" individual, Morrell and Parsons⁹ conclude, in part, that the search for a unique personality configuration associated with coronary disease has been "disappointingly unproductive," and that insufficient attention has been paid to age, sex, socioeconomic status (SES) and other critical attributes. They call attention, however, to the fact "...that several sources of evidence have demonstrated that psychological stress is implicated in CAD [coronary artery disease]"; and to the "important empirical data" of Friedman and Rosenman, "...which await a systematic theoretical treatment." Finally, they suggest: "It is most probable that the well-established hereditary determination of CAD...and sociocultural factors will be the vehicles through which the contribution of

This discussion is intended as an informative review only, and is not meant to imply a recommendation for any drug or other specific therapy by its content or by the authors cited.



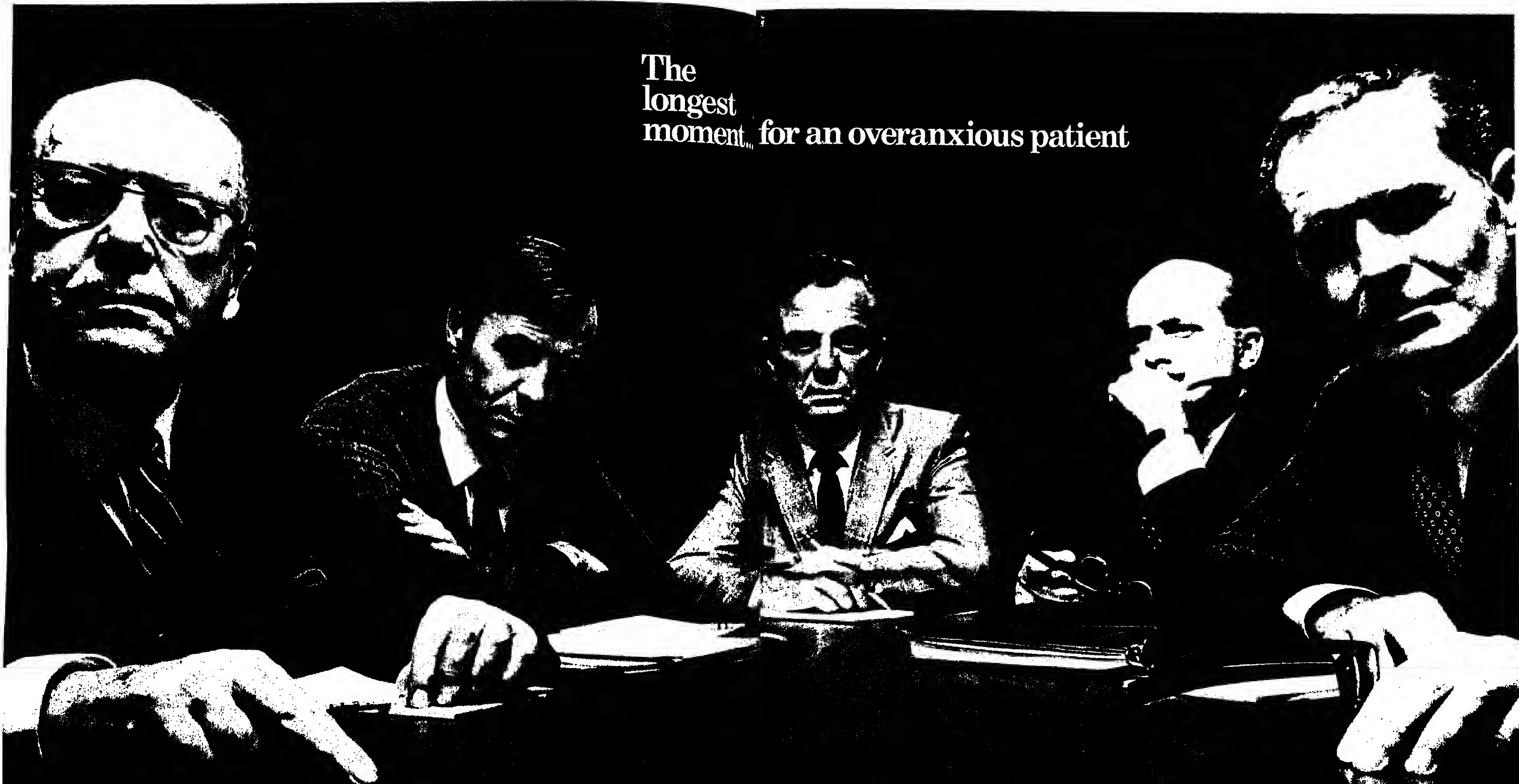
Pattern Type A is an aggressive individual who must assert himself as one who deserves recognition and good service, whether from fellow-workers or a waiter. Pattern Type A has been associated with a significantly higher incidence of CHD as compared to other patients with the same coronary risk factors.

Pattern Type B may be too self-effacing to stand up for his rights even in small matters. He is the sort that often lets himself get "beaten out" of his place in line or will yield the cab he has hailed to someone more aggressive. The incidence of CHD for Pattern B is no greater than that for the general at-risk population.



Please see page 8 of this advertisement for important prescribing information.

The longest moment... for an overanxious patient



At moments of high importance to the individual, intense anxiety can paralyze positive response. It is a truism that adequate preparation contributes to effective task performance. Even so, the anxiety-ridden individual—however capable—and prepared—is not immune to apprehensive imaginings or excessive emotional tension. When the stakes are high, when the potential threat to status and self-esteem is considerable, anxiety

must be kept at low levels to assure optimal mental function.

In a recent conference on psychological stress, one participant* distinguished between "coping" and "defense." *Coping*, in his view, "refers to the instrumental behavior and instrumental capacities in meeting life demands and goals. It involves the application of skills, techniques, and knowledge that a person has acquired." *Defense*, on the other hand, "refers to the manner in which a person

manages his emotional and affective states when discomfort is aroused or anticipated." Mastery in a given situation depends to a large extent on the person's ability to mobilize his needed efforts, on his skill in dealing with tasks and people and on his own assessment of perception of his abilities. Uncertainty in this regard can quickly lead to the immobilizing confusion engendered by extreme anxiety.

Librium (chlordiazepoxide HCl)

- can provide prompt antianxiety action.
- can be useful for undue anxiety associated with a wide range of functional and organic disorders.
- generally does not unduly interfere with mental acuity, on proper maintenance dosage.
- has demonstrated a wide margin of safety in more than eleven years' clinical

use. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated. (See full prescribing information.)

*Mechanic, D.: Invited commentary, in Appleby, M. H., and Trumbull, R. (eds.): *Psychological Stress: Issues in Research*, New York, Appleton-Century-Crofts, Div., Meredith Publishing Co., 1967, pp. 201,202.

for moderate to severe anxiety that can block effective response

Librium® 10mg
(chlordiazepoxide HCl)
1 or 2 capsules
t.i.d./q.i.d.

Please see page 8 of this advertisement for important prescribing information.

Librium® and Libritabs® (chlordiazepoxide HCl) (chlordiazepoxide) 5-mg, 10-mg, 25-mg capsules 5-mg, 10-mg, 25-mg tablets up to 100 mg daily for severe anxiety



for prompt relief of varying levels of excessive anxiety

Since anxiety levels vary even in the same patient, oral Librium (chlordiazepoxide HCl) is made available in three different dosage strengths.

For mild or moderate anxiety, Librium is recommended in lower dosages of 5 or 10 mg t.i.d. or q.i.d.

For the patient in acute emotional distress due to severe anxiety, 25 mg Librium t.i.d. or q.i.d. is usually effective and convenient.



Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Descriptions: Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) are versatile therapeutic agents of proven value for the relief of anxiety and tension. Librium (chlordiazepoxide HCl) Capsules and Libritabs (chlordiazepoxide) are useful for prompt, effective relief of common emotional disturbances. Librium (chlordiazepoxide HCl) is the first of a new class, unrelated chemically and pharmacologically to other types of tranquilizers. Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) promptly relieve anxiety and tension over a wide range of emotional disorders, and are among the safest of the effective psychopharmacologic compounds available.

Librium (chlordiazepoxide HCl) Capsules
Injectable Librium (chlordiazepoxide HCl)

With respect to clinical activity, the base of chlordiazepoxide and its hydrochloride salt are indistinguishable and may be used interchangeably on a milligram-for-milligram basis.

Chlordiazepoxide is 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide hydrochloride. A colorless, crystalline substance, it is soluble in water. It is unstable in solution and the powder must be protected from light. The molecular weight is 336.22.

Libritabs (chlordiazepoxide) tablets provide the psychotropic action of Librium (chlordiazepoxide HCl). The relationship between Libritabs (chlordiazepoxide) and other dosage forms containing chlordiazepoxide HCl is as follows:

Libritabs (chlordiazepoxide) Tablets
Injectable Librium (chlordiazepoxide HCl) Capsules
With respect to clinical activity, the base of chlordiazepoxide and its hydrochloride salt are indistinguishable and may be used interchangeably on a milligram-for-milligram basis.

Chlordiazepoxide is 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide. It is a slightly yellow, crystalline material and is insoluble in water. The molecular weight is 336.22. Animal Pharmacology: The drug has been studied extensively in many species of animals and these studies are suggestive of action on the limbic system of the brain.^{1,2,3} which recent evidence indicates is involved in emotional responses.^{4,5}

Hostile monkeys were made tame by oral drug doses which did not cause sedation. Chlordiazepoxide HCl revealed a "taming" action of the elimination of fear and aggression.⁶ The taming effect of chlordiazepoxide HCl was further demonstrated in rats made vicious by lesions in the septal area of the brain. The drug dosage which effectively blocked the vicious reaction was well below the dose which caused sedation in these animals.⁷

The oral LD₅₀ of single doses of chlordiazepoxide HCl, calculated according to the method of Miller and Tainter,⁸ is 720±51 mg/kg as determined in mice observed over a period of five days following dosage.

The oral LD₅₀ of single doses of chlordiazepoxide, calculated according to the method of Miller and Tainter,⁸ is 860±76 mg/kg as determined in mice observed over a period of five days following dosage.

Effects on Reproduction: Reproduction studies in rats fed chlordiazepoxide HCl, 10, 20 and 80 mg/kg daily and bred through one or two matings showed no congenital anomalies, nor were there adverse effects on lactation of the dams or growth of the newborn. However, in another study at 100 mg/kg daily there was noted a significant decrease in the fertilization rate and a marked decrease in the viability and body weight of offspring which may be attributable to sedative activity, thus resulting in lack of interest in mating and lessened maternal nursing and care of the young.^{9,10} One neonate in each of the first and second matings in the rat reproduction study at the 100 mg/kg dose exhibited major skeletal defects. Further studies are in progress to determine the significance of these findings.

Indications: Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) are indicated when anxiety, tension and apprehension are significant components of the clinical profile.

In low oral doses, Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) are useful in the relief of mild and moderate anxiety, and tension occurring alone or in association with gastrointestinal, cardiovascular, musculoskeletal, gynecologic, dermatologic disorders and anxiety reactions in children over age five. (See Dosage.)

Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) are effective in the relief of preoperative apprehension and may be administered for several days prior to or immediately preceding the operative procedure. (See Dosage.)

In higher oral doses, Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) are also useful in the relief of the more severe anxiety and tension states, alone or associated with organic disorders or psychoneurotic reactions. They may be

useful as adjunctive therapy in some psychoses where anxiety and tension are present,¹¹ and in agitation due to chronic alcoholism or alcohol withdrawal with or without delirium tremens.

Contraindications: Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide) are contraindicated in patients with known hypersensitivity to the drug.

Warnings: As in the case of other CNS-acting drugs, patients receiving Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) should be cautioned about possible combined effects with alcohol and other CNS depressants.

As is true of all preparations containing CNS-acting drugs, patients receiving Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) should be cautioned against hazardous occupations requiring complete mental alertness such as operating machinery or driving a motor vehicle.

Physical and Psychological Dependence: Physical and psychological dependence have rarely been reported in persons taking recommended doses of Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide). However, caution must be exercised in administering Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) to individuals known to be addicted to drugs or those whose history suggests they may increase the dosage on their own initiative. Withdrawal symptoms following discontinuation of chlordiazepoxide hydrochloride have been reported.¹² These symptoms (including convulsions) are similar to those seen with barbiturates.

Usage in Pregnancy: Use of any drug in pregnancy, lactation, or in women of childbearing age requires that the potential benefit of the drug be weighed against its possible hazards to the mother and child. (See Animal Pharmacology.)

Management of Overdosage: Manifestations of Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) overdosage include somnolence, confusion, coma and diminished reflexes. Respiration, pulse and blood pressure should be monitored, as in all cases of drug overdosage, although, in general, these effects have been minimal following Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) overdosage. General supportive measures should be employed along with immediate gastric lavage. Intravenous fluids should be administered and an adequate airway maintained. Hypotension may be combated by the use of Levophed® (levorphanol) or Aramine (metaraminol). Ritalin (methylphenidate) or caffeine and sodium benzoate may be given to combat CNS-depressive effects. Dialysis is of limited value. There have been occasional reports of excitation in patients following chlordiazepoxide HCl or chlordiazepoxide overdosage; if this occurs, barbiturates should not be used. As with the management of intentional overdosage with any drug, it should be borne in mind that multiple agents may have been ingested.

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to the smallest effective amount to preclude the development of ataxia or oversedation (10 mg or less per day initially, to be increased gradually as needed and tolerated). In general, the concomitant administration of Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) and other psychotropic agents is not recommended. If such combination therapy seems indicated, careful consideration should be given to the pharmacology of the agents to be employed—particularly when the known potentiating compounds such as the MAO inhibitors and phenothiazines are to be used. The usual precautions in treating patients with impaired renal or hepatic function should be observed.

Paradoxical reactions, e.g., excitement, stimulation and acute rage, have been reported in psychiatric patients and in hyperactive, aggressive children, and should be watched for during Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) therapy. The usual precautions are indicated when Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) is used in the treatment of anxiety states where there is any evidence of impending depression; it should be borne in mind that suicidal tendencies may be present and protective measures may be necessary. Although clinical studies have not established a cause and effect relationship, physicians should be aware that variable effects on blood coagulation have been reported very rarely in patients receiving oral anticoagulants and chlordiazepoxide HCl.

Adverse Reactions: The necessity of discontinuing therapy because of undesirable effects has been rare.¹³ Orowsiness,¹⁴ ataxia¹⁵ and confusion¹⁶ have been reported in some patients—

particularly the elderly and debilitated.¹⁷ While these effects can be avoided in almost all instances by proper dosage adjustment, they have occasionally been observed at the lower dosage ranges. In a few instances syncope has been reported.¹⁸ Other adverse reactions reported during therapy include isolated instances of skin eruptions,¹⁴ edema,¹⁷ minor muscular irritabilities,¹⁴ nausea and constipation,¹⁶ extrapyramidal symptoms,¹⁹ as well as increased and decreased libido. Such side effects have been infrequent and are generally controlled with reduction of dosage. Changes in EEG patterns (low-voltage fast activity) have been observed in patients during and after chlordiazepoxide HCl treatment.²⁰

Blood dyscrasias, including agranulocytosis,²⁰ jaundice and hepatic dysfunction,²¹ have occasionally been reported during therapy. When Librium (chlordiazepoxide HCl) or Libritabs (chlordiazepoxide) treatment is protracted, periodic blood counts and liver function tests are advisable.

Dosage and Administration: Because of the wide range of clinical indications for Librium (chlordiazepoxide HCl) and Libritabs (chlordiazepoxide), the optimum dosage varies with the diagnosis and response of the individual patient. The dosage, therefore, should be individualized for maximum beneficial effects.

Adults
Relief of mild and moderate anxiety and tension
Relief of severe anxiety and tension

Usual daily dose
5 mg or 10 mg, 2 to 4 times daily
20 mg or 25 mg, 3 or 4 times daily
5 mg, 2 to 4 times daily

Geriatric patients, or in the presence of debilitating disease
Preoperative Anesthesia: On days preceding surgery, 5 to 10 mg orally 3 or 4 times daily. If used as preoperative medication, 50 to 100 mg i.m.* one hour prior to surgery.

Children
Because of the varied response of children to CNS-acting drugs, therapy should be initiated with the lowest dose and increased as required. Since clinical experience in children under 6 years of age is limited, the use of the drug in this age group is not recommended.

In acute agitation, alone or associated with chronic alcoholism and alcohol withdrawal (including delirium tremens), the parenteral form* is usually used initially. If the drug is administered orally, the suggested initial dose is 50 to 100 mg, to be followed by repeated doses as needed until agitation is controlled—up to 300 mg per day. Dosage should then be reduced to maintenance levels.

*See package insert for Injectable Librium (chlordiazepoxide HCl).

How Supplied: Capsules: containing 5 mg chlordiazepoxide hydrochloride, green and yellow, bottles of 100 and 500; containing 10 mg chlordiazepoxide hydrochloride, green and black, bottles of 100 and 500; containing 25 mg chlordiazepoxide hydrochloride, green and white, bottles of 100 and 500. All strengths also available in Tal-E-Oose® packages of 1000.

Tablets: containing 5 mg, 10 mg, or 25 mg chlordiazepoxide, bottles of 100 and 500.

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THIS PRODUCT INFORMATION, ISSUED SEPTEMBER 1971.



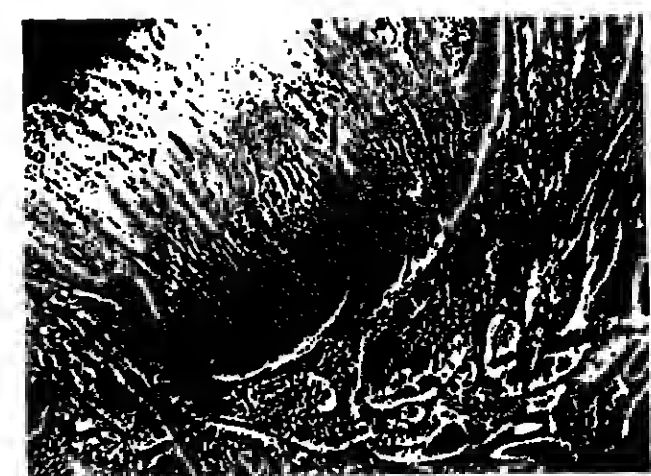
gs is also carried out.



rating dialysis machine. He had taken 10 mgals expect the present rate of home .0 per cent, to double in five years.



nts at Baylor College of Med- ical study program for college stu- expose participants to clinical t medical school admissions chal Young check an infant.



Liver culture after 20 days. Bundles of pulsating cells radiate from liver explant (dark area) and form monolayer.



Most common cell type seen in primary liver cultures.

The Adult Human Liver Is Studied in Tissue Cultures

ADULT HUMAN LIVER biopsy specimens were cultured to observe growth and ascertain whether the in vitro characteristics of these cells were related to histologic lesions in the patient's organ, by Charles Demoise and Arthur Falck, both Ph.D.s, and Dr. John Galambos, at the Emory University School of Medicine.



DR. FALCK



DR. DEMOISE



DR. GALAMBOS

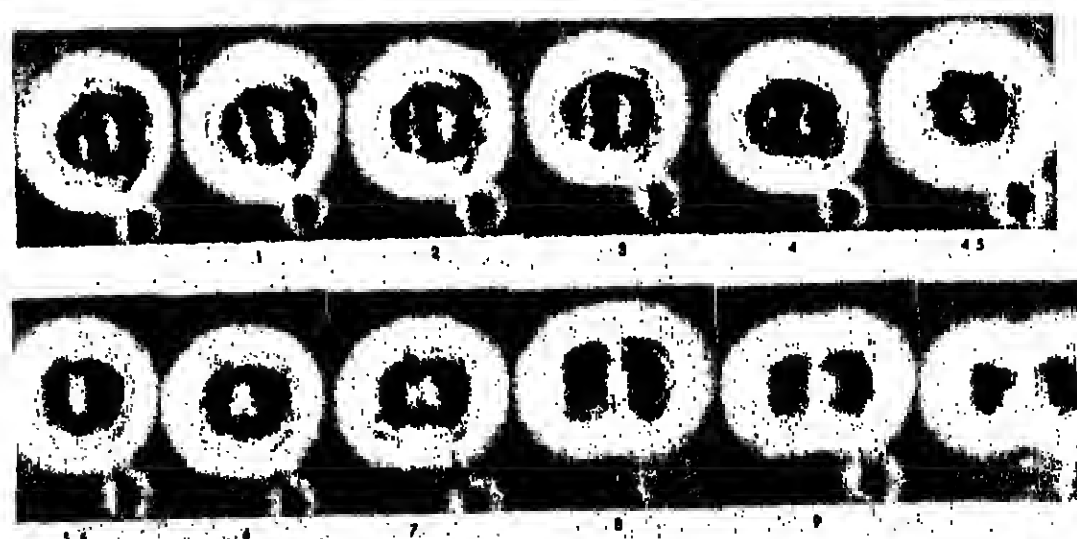
Results indicated that cells obtained from persons with alcoholic or viral hepatitis had higher growth and survival rates than those cultured from morphologically normal or fatty livers. In addition, cultures obtained from normal cells were more difficult to subculture.



Metaphase stage, apparently normal, of cell occurring in 200 mg. ethanol per 100 ml of culture media.



Binucleate cell resulting from karyoplasmic constriction.



Sequence of liver culture cell in mitosis. Nine minutes elapsed from metaphase stage to daughter cell.

Hospital Society Backs President On Wage Freeze

Continued from page 1

"But it may mean a lot more than that after 90 days," Mr. Hahn added.

Even before the 90 days is up, however, he said, he is "sure that some hospitals will provide new services . . . and will have to price those services according to the rules set out by the Government." Rulings will also be required in some questions of salaries and house officer stipends, he said.

The A.H.A. registry lists more than 7,000 hospitals with nearly 3,000,000 employees, full- and part-time. In the U.S. the association said that the freeze halted some scheduled wage increases before they went into effect but in other "numerous cases the hospitals have already granted and paid" wage increases without yet implementing a rate boost.

For Wesley Memorial Hospital here the "bind" is not wages, its spokesman said, but a \$1,000,000 electrical renovation contract plus about \$750,000 to cover promised improvements in employee health and disability insurance and stipends for more interns. The hospital is a training facility for Northwestern University, which is asking a 25 per cent expansion in the intern roster next year and already has scheduled a 16 per cent expansion this year—"at \$10,500 per intern," the spokesman said.

Costs Would Have Risen

The contracted expenses, construction and otherwise, were to have been covered at Wesley by a September 1 rate increase that would have raised the \$66 per-patient daily cost in a double room to \$77. In addition, Wesley employees were to get wage increases September 1. The freeze stopped both planned rises but not the previous contractual obligations.

Adding to the financial problems at Wesley is an empty bed situation due partly to the usual summer slow-down and partly to the fact that electrical work on the 16-story building requires removal of patients from an entire floor at any one time.

The hospital spokesman said the 12 per cent payroll cut was "in money, not people" and probably would affect fewer than 12 per cent of the 1,600 full-time employees.

An A.H.A. official said the Wesley Memorial situation might be "one of many" for which specific queries could be made at the Office of Emergency Preparedness. The A.H.A. role in liaison with OEP, President Hahn said, possibly would include such knotty questions as "utilization, which controls costs," and the processing of "complaints by patients."

Does Not Expect Complaints

Mr. Hahn said he does "not expect complaints from hospitals" during the relatively short period of the freeze. A.H.A. president-elect, Stephen M. Morris, president of Good Samaritan Hospital in Phoenix, Ariz., said he thought that "the OEP guidelines would be enforced voluntarily" because "so much public pressure would be engendered by a rate rise during the freeze."

However, said Mr. Morris, the costs of running a hospital will not be held down completely by the wage-price freeze and "readjustments will have to come" in the postfreeze period.

On the same subject, Elliot L. Richardson, U.S. Secretary of Health, Education, and Welfare, warned the A.H.A. in an address that "this is the time to face the fact that after 90 days it will not be desirable to return to 'inflation as usual.'" He urged health care leaders to use the time "to consider the steps it will take to reduce inflation in the future with as little Government intervention as possible."

Asked about the possibility of exempting hospitals from the freeze, Mr. Richardson told a few conferees that it was "only fair that everyone should be included" during the first phase of the Administration's anti-inflation campaign.

Liver Scanning in Cancerous Held of Doubtful Specificity

Continued from page 1

for therapy or prognosis unless it is normal, the investigators said. A normal scan, they said, reflects a better prognosis and aids the clinician in his approach to therapy, especially if radical surgery is a consideration.

"An abnormal scan," they went on, "is nonspecific whether the abnormality is focal or diffuse; metastases may or may not be present. Liver function studies are even less sensitive and equally nonspecific with one exception. Where the alkaline phosphatase is markedly elevated, bone disease and biliary obstruction is excluded, and a focal defect is noted on the scan, the presence of hepatic metastases is virtually certain."

"Percutaneous liver biopsy or laparotomy and inspection are specific only when positive. Indeed, percutaneous liver biopsy or hepatic visualization at laparotomy will fail to detect tumor in 30 to 40 per cent of cases."

"These facts suggest an approach to the evaluation of the liver for metastases in cancer patients. An abnormal scan is an indication for liver biopsy. This may be

danced percutaneously or under direct visualization at laparotomy. If a focal defect is present on scan, that area should be biopsied, if possible.

"If the biopsy is normal, a laparotomy with biopsy of visible lesions should be performed, but if no lesions are seen a generous wedge of tissue should be obtained. This approach would appear to offer the greatest opportunity of detecting metastatic hepatic disease."

No Prognostic Tie of Symptoms, Survival in Renal Cancer Seen

From Mass. General Hospital

► No significant prognostic relationship could be found between various presenting symptoms or laboratory abnormalities and overall survival in a series of 309 cases of renal cell carcinoma surgically treated at Massachusetts General Hospital during a 30-year period, the meeting was told.

Division by pathologic stage correlated better with survival than did division by histologic grade, but both were important determinants in predicting prognosis of individual cases, according to Drs. Donald

When meditating over a disease, I never think of finding a remedy for it, but, instead, a means of preventing it.

Louis Pasteur (1822-95)
Address to the Fraternal Association of Former Students of the Ecole Centrale des Arts et Manufactures, Paris, May 15, 1884.

G. Skinner, Robert B. Colvin, Clinton D. Vernillion, Richard C. Pfister, and Wynd F. Leebetter.

Grading was based solely on nuclear morphology in order to simplify it, they said. This method of grading had definite, although limited, predictive value within stages 1, 3, and 4, they found. Pure clear-cell carcinomas had a better prognosis than granular and mixed forms up to five years, and spindle-cell types had the worst prognosis.

Operative mortality in the series was 5 per cent, and over-all survival was 44 per cent at five years and 33 per cent at 10 years.

Excluding those patients with metastases present when first seen for treatment, five-year survival was 57 per cent and 10-year survival was 44 per cent, the physicians said.

Artificial Kidney Featured at State Fair



Central New York Regional Medical Program sponsored an artificial kidney exhibit at the N.Y. State Fair in Syracuse, N.Y. Cathie Smith, R.N., Jan Metcary, R.N., both of Johnson City, and Walter Curry, RMP teaching coordinator, man the equipment. They also illustrated donor care and transplant information. Officially estimate that there are 800 hemodialysis patients throughout the state.

Unit Traces Esophagus Cancer By Study of Alcoholic Drinks

Continued from page 1

in some parts of Russia than it is in Ceylon. Cancer incidence tends to make broad geographical patterns, but cancer of the esophagus tends to occur in what might be called spots."

The agency's liaison man is Dr. Janec Kmet, a Yugoslav physician. "The two areas of highest incidence in Europe are France and Switzerland, with France having the highest rate," he pointed out to MEDICAL TRIBUNE. "The age-standardized esophageal cancer mortality rate per 100,000 population per year for males in 1965-66 in France was 13.7 and in Switzerland 9.22."

The investigator noted, however, that rates for the 21 regions of France show that the male esophageal cancer mortality is by no means the same throughout the country but varies considerably from one region to another. "The highest rates are in Brittany. Both maps bear a striking resemblance to maps showing alcoholism rates. A computer study has confirmed the relationship."

In the more detailed map, by small de-

partments rather than large regions, there is a close relationship between deaths attributed to alcoholism and cancer of the esophagus and a much lower relationship between cirrhosis of the liver and mortality from cancer of the esophagus.

"We now know," said Dr. Tuyns told MEDICAL TRIBUNE, "that there is no department in France with a high rate of cancer of the esophagus that does not also have a high rate of alcoholism. But in some departments the rate of alcoholism is high but there is no notable increase in male deaths from cancer of the esophagus. This is true, for example, in the departments of the Ardennes, Haute Savoie, and Savoie."

In Poland, where cancer of the esophagus is not common, the national drink is vodka, which is simpler in composition than most other alcoholic drinks.

Beverages Collected

The IARC has now collected and bottled locally brewed beverages from Jamaica, Curacao, Puerto Rico, Iran, Brittany, and Singapore. The contents of these samples will be tested for the presence of carcinogenic compounds, particularly nitroamines, at the British Food Manufacturers' Industrial Research Association laboratories in Leatherhead, Surrey, under the direction of Dr. C. L. Walters.

In Europe, as in most but not all areas of the world, esophageal cancer is more prevalent in males than in females. For reasons not understood, the highest mortality for females in Europe does not occur in France, the country with the highest male mortality, but in Eire.

Many questions remain about cancer of the esophagus in Europe; why is it notably more common among males than females except in Finland and Northern Ireland (but where in some years women have had equal or higher rates) and in Eire, where the female mortality is rising and the male mortality declining? And why in at least three countries—Denmark, Finland, and Switzerland—is there, as Dr. Tuyns puts it, "a decrease which may be considered as a real phenomenon?"

In Asia, IARC statistics indicate that there is an "esophageal cancer belt" stretching from north of Korea, crossing Mongolia as it moves west, and passing through a large part of the Soviet Union, including Turkmenistan and the Uzbek Soviet Socialist Republic. It then moves further westward, through the northern part of Iran, and peters out around the border of Turkey. But along the southern tip of the Caspian Sea, yet very much in the "cancer belt," there is a small area of extremely low incidence, adjacent to an area of high incidence and less than 100 miles from an area of extremely high incidence. There is, in effect, an "island" of relative safety.

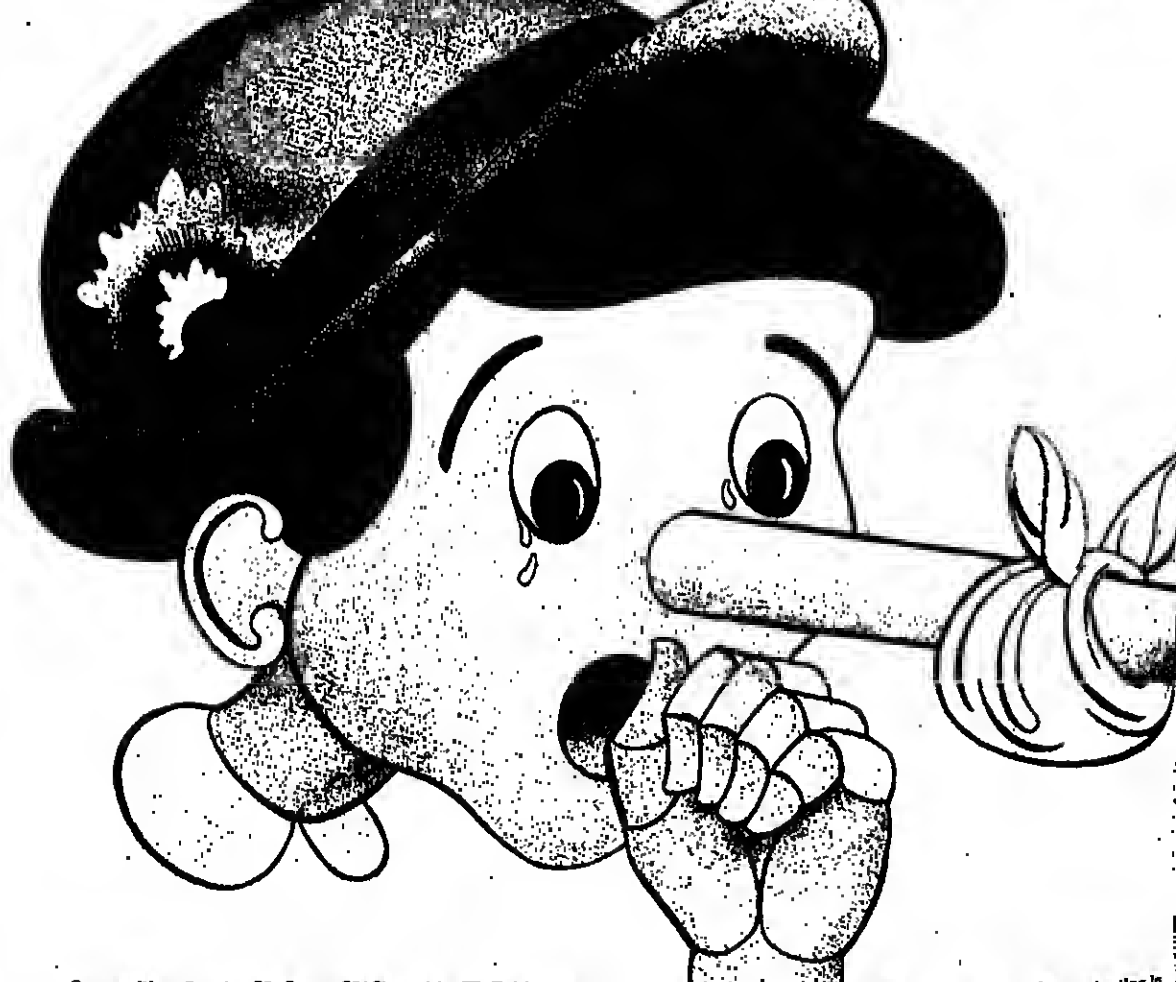
Wide Range of Incidence

A survey of the region beginning in July, 1968, and concluding in June, 1970, resulted in the establishment of annual incidence (amplified age-adjusted) for ages 35 through 64 in areas of Iran near the southern end of the Caspian Sea. These ranged from as high as 272.1 per 100,000 among males and 412.6 among females in some districts to as low as 18.6 for males and 6.6 for females in others.

Studies of difference in habits, and other factors, between high- and low-incidence areas are continuing. "Where a tumor is as frequent as cancer of the esophagus in Iran," Dr. Kmet commented, "it is probable that the environmental hazard is widespread. But the environmental hazard is not necessarily a specific carcinogenic substance. In the high-incidence areas there could be a general deficiency which predisposes the people to this kind of cancer."

Preliminary studies to determine the role of alcohol, tobacco, and opium in cancer of the esophagus in Iran indicate that such factors can virtually be ruled out, the investigators said.

The Cold Truth about Stuffy Noses and Coughs



Children do well with an oral decongestant

Typical decongestants work fast, but don't go far enough. They don't shrink all the nasal and sinus tissues.

Rondec Soral decongestant shrinks mucous membranes and blocks histamine response

Shrinking mucous membranes from the tip of the nose down to the bronchi, pseudoephedrine is apparently more specific than ephedrine for the vessels of the respiratory tract. But it has fewer side effects. Pressor action is minimal. Significant CNS stimulation is rare. It doesn't cause rebound congestion or irritation.

Carbinexamine has a high level of antihistamine activity. And while sedation may occur, it is generally mild and transient—shouldn't give a school-age child that wooden-headed feeling.

Rondec-DM adds cough control that's non-narcotic

The dextromethorphan hydrobromide in Rondec-DM controls unproductive cough without the constipation and respiratory depression associated with narcotics. Drowsiness or gastrointestinal upsets rarely occur. And glyceryl guaiacolate works to thin bronchial secretions. Two products for dependable relief of cold symptoms. Two good flavors kids like. And a low incidence of side effects.

That's the long and short of it.

cut cold symptoms down to size

for stuffy noses:
Rondec S[®] Syrup

60 mg pseudoephedrine HCl and 2.5 mg carbinexamine maleate per 5 ml

for cough with a cold:
Rondec-DM[®] Syrup

15 mg dextromethorphan HBr, 100 mg glyceryl guaiacolate, 60 mg pseudoephedrine HCl, and 2.5 mg carbinexamine maleate per 5 ml



carbinexamine maleate. However, it is generally mild and tolerance appears to develop rapidly in most cases. Patients particularly sensitive to antihistamines may experience moderate or severe drowsiness.

Mild gastrointestinal disturbances and drowsiness have been observed among patients receiving dextromethorphan hydrobromide or glyceryl guaiacolate. These instances are rare, and no serious side effects have been reported. Patients should be cautioned to exercise care in driving or operating machinery until the possibility of drowsiness is determined. If a sensitivity reaction or idiosyncrasy should occur, reduce dosage or withdraw the drug.

Administration and Dosage: Clinical trials among series of infants and children indicate that the usual dosage frequency of four times daily is effective and well tolerated. Because response to the ingredients will vary according to the illness and type of patient under treatment, dosage should be adjusted by the age and clinically determined needs of the individual patient. In mild cases, dosage and/or frequency may be reduced.

Dosage Schedule:

Age	Rondec S Syrup	Rondec-DM Syrup	Frequency
1-3 mos	1/4 dropperful	1/4 dropperful	q.i.d.
4-6 mos	1/4 dropperful	1/4 dropperful	q.i.d.
7-9 mos	1/4 dropperful	1/4 dropperful	q.i.d.
10-18 mos	1 dropperful	1 dropperful	q.i.d.

Precautions and Side Effects: Although pseudoephedrine causes virtually no pressor effects in normal individuals, patients with caution in hypertension. While the majority of patients will experience no side effects from pseudoephedrine hydrochloride, those particularly sensitive to sympathomimetic amines may note mild stimulation. Sedation has been observed in connection with the use of

Complaints: Rondec S[®] Syrup, Chewable, T[™] Tablet contains 2.5 mg carbinexamine maleate, 60 mg pseudoephedrine hydrochloride per 5 ml (teaspoonful) tablet. Rondec-DM[®] Syrup contains the above plus 15 mg dextromethorphan hydrobromide, 100 mg glyceryl guaiacolate, 5.5 mg chlorpheniramine (some loss unavoidable), alcohol less than 0.6% per 5 ml (teaspoonful). Rondec-DM[®] Drops contains 1 mg carbinexamine maleate, 30 mg pseudoephedrine hydrochloride per 1 ml dropperful. Rondec-DM[®] Tablets contains the above plus 4 mg dextromethorphan hydrobromide, 20 mg glyceryl guaiacolate, 0.7 mg chlorpheniramine (some loss unavoidable), alcohol less than 0.6% per 1 ml dropperful.

Action and Uses: Carbinexamine maleate is an antihistamine drug with a therapeutic index ratio of median lethal dose to median effective dose in guinea pigs that is 2 to 30 times that of chlorpheniramine, pheniramine, diphenhydramine and triphenylamine. Carbinexamine maleate has a low incidence of side effects, particularly the sedation associated with these agents. Sedation when it occurs is generally mild and transient.

Pseudoephedrine decongests swollen mucous membranes of the respiratory tract by vasoconstriction and opens obstructed airways through direct action on the smooth muscles of the bronchi. While the vasoconstrictive action of pseudoephedrine is similar to that of ephedrine, it seems to be more specific for the blood vessels of the respiratory tract and less specific for the systemic circulation. Pseudoephedrine has been shown in clinical and laboratory tests to have minimal pressor effect at usual dosages. Dextromethorphan hydrobromide has been demonstrated in clinical trials to produce an antitussive effect equal to that of codeine. It acts centrally to elevate the cough threshold. The incidence of side reactions in long-term clinical trials has been remarkably low and no greater than that occasioned by placebo. There is no liability of addiction. At usual dosage it will not depress respiration or inhibit allergy activity. Glyceryl guaiacolate has been shown to increase the rate of

respiratory tract fluid production in animals when administered orally. This action reduces the viscosity of bronchial secretions. Although similar objective measurements have not been accomplished in humans, clinical studies in adults and children indicate it is an effective expectorant with virtually no adverse reactions. The available evidence suggests that glyceryl guaiacolate has a direct effect on bronchial secretory glands following absorption into the bloodstream.

Indications: Rondec S[®] and T[™] are indicated when histamine blocking, mucosal decongestion and bronchodilation are desired in upper and lower respiratory tract disorders of allergic, infectious or nonspecific aetiology: common cold - allergic rhinitis - nasopharyngitis - sinusitis - otitis media - eustachian tube obstruction - bronchitis - tracheitis - laryngitis - croup.

In patients with nasopharyngitis and a history of otitis media and T[™] or Rondec-DM as adjunctive therapy to antibiotics and T[™] or Rondec-DM as adjunctive therapy to antibiotics when relief of mucosal congestion and cough is desired. Rondec-DM is indicated when control of unproductive cough and mucosal decongestion are desired in the following respiratory disorders:

• allergic cough • recurrent cough due to recurrent respiratory infection • bronchitis and bronchial cough • nasopharyngitis with postnasal drip • common cold. There is no known contraindication to the use of Rondec S[®] and T[™] or Rondec-DM as adjunctive therapy to antibiotics when relief of mucosal congestion and cough is desired. Precautions and Side Effects: Although pseudoephedrine causes virtually no pressor effects in normal individuals, patients with caution in hypertension. While the majority of patients will experience no side effects from pseudoephedrine hydrochloride, those particularly sensitive to sympathomimetic amines may note mild stimulation. Sedation has been observed in connection with the use of

An FDA Warning Asked on Toxicity Of Methotrexate

Medical Tribune Report
Washington Bureau

WASHINGTON—The Food and Drug Administration should warn the medical profession of the high toxicity of methotrexate—the potent anticancer agent that has found widespread use in the United States for psoriasis—according to Rep. L. H. Fountain (D.-N.C.).

The agency should also make it clear that use of methotrexate for psoriasis without an Investigational New Drug exemption causes the drug to be legally misbranded and jeopardizes its availability even for legitimate purposes, Mr. Fountain said in a letter to Dr. Charles C. Edwards, FDA Commissioner.

The chairman of the House Intergovernmental Relations Subcommittee of the Committee on Government Operations remarked that "the legal impact of the physicians' unauthorized use of approved new drugs does not seem to be generally known to the medical profession."

"Editorials such as that which appeared in the July 12, 1971, issue of the *Journal of the American Medical Association* serve to encourage the unauthorized use of drugs by stating that FDA's insistence upon INDs has no basis in law," he declared.

If FDA notified physicians that use of approved drugs for nonapproved purposes might have the effect of depriving all patients of these drugs, Mr. Fountain said, physicians would be encouraged to file INDs.

An explicit warning in the labeling against use of methotrexate for psoriasis except on an investigational basis would probably deter physicians from the improper use of this drug, he told Dr. Edwards.

Hope to Approve Labeling

At recent hearings, FDA officials said they hoped to resolve the methotrexate problem by approving some form of labeling for the use of the drug in psoriasis.

Mr. Fountain asserted, however, that "there still appear to be fundamental, unresolved questions concerning the safety of methotrexate for psoriasis which raise doubts as to whether the Food and Drug Administration can at this time draw any firm conclusions about the safety of such use."

The letter cited testimony before the subcommittee by Dr. Henry H. Roenigk, Jr., of the Cleveland Clinic department of dermatology, that the 25 deaths known to FDA from use of methotrexate in psoriasis represent a small portion of the actual number of fatalities, on the basis of his own experience and that of others whose work he has surveyed.

The problem of what to do about methotrexate, Mr. Fountain noted, is further complicated by the fact that the manufacturer, Lederle Laboratories, is requesting withdrawal of its supplemental new drug application for use of the product in psoriasis. The methotrexate situation, he charged, "is a classic example of FDA's failure to act early and decisively."

Smallpox Wanes in India

Medical Tribune World Service

NEW DELHI—The incidence of smallpox in India has dropped to the lowest level in history, the Government announced here. Complete figures for 1970 showed 10,055 cases and 1,805 deaths, compared with 19,120 cases and 4,154 deaths in 1969.

A typographic omission occurred in a MEDICAL TRIBUNE report (August 18) listing the cost to physicians to enroll for home study tests and syllabus sets prepared by the American College of Radiology. To A.C.R. members the cost is \$45; to nonmembers, \$65; to residents, \$35.

Cholesterol Held Essential As Nerve Impulse Mediator

Medical Tribune Report

UPTON, N.Y.—Cholesterol has been found to be essential as a mediator for the conduction of all nerve impulses throughout the body, according to a report from Brookhaven National Laboratory.

The finding was described as an unexpected result of the use of new cryobiological methods for tissue research pioneered at this laboratory by a group headed by Simon Freed, Ph.D. Dr. Freed officially retired in 1965 but remains active as a research collaborator in the laboratory's chemistry department and as a Research Professor at the New York Medical College.

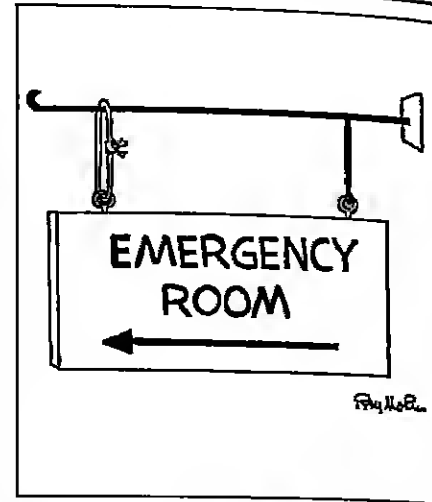
Combining research at both institutions, Dr. Freed, together with Dr. Tetsuya Noguchi, who is on leave from Keio University, Tokyo, developed the new method of cryoextraction-reconstitution for the study of nerve cell membrane enzymes. This is said to be the only known way to separate the fatty and protein components of enzyme molecules without destroying the enzymatic viability.

The membrane enzyme mainly studied was sodium-potassium-stimulated adeno-

sine triphosphatase. It surrounds all nerve cells in the brain and elsewhere, mediates energy required for nerve conduction, and is essential for all activity of the nervous system, both from and to the brain, the Brookhaven report said.

The first step was to "instant-freeze" the brains of rats, obtained from Brookhaven's medical research center, in liquid nitrogen at -196° C. The temperature of the brain tissue containing the enzyme was then raised to -75° C. The lipids were then dissolved by a mixture of 50 per cent chloroform and 50 per cent methyl alcohol already at -75° C. The mixture was filtered at this temperature, allowing the dissolved lipids to pass through the filter while the proteins stayed behind in the residue.

The lipid extract was then fractionated into its various components and individually recombined at -75° C. with the protein component, which by itself is inactive as an enzyme. It was found that only cholesterol restored virtually full enzymatic activity. Other lipid components, such as phosphatidyl choline, phosphatidyl serine, and phosphatidyl chloride, were



about one-fourth or less as effective as cholesterol in the restoration of enzymatic activity.

Certain well-known cardiac glycosides are specific enzyme inhibitors of sodium-potassium-stimulated adenosine triphosphatase, the Brookhaven report said. These glycosides contain, as part of their molecules, structures similar in size and shape to cholesterol. The investigators postulated that these glycosides act as inhibitors because they can compete with cholesterol and displace it from its site on the enzyme molecule.

Considering a change in the way you treat obesity?



September

Many physicians are currently changing their approach to the treatment of the obese patient and their choice of an anorexic agent. One approach, for example, involves the increasing realization that losing weight requires patience.

Since obesity can be a serious threat to health, it should be treated by every physician. Treatment should give early motivation and give the patient time to adjust to new eating and exercise habits.

For some, this change in treatment will include a change in the anorexic used as adjunctive support during indicated periods of time. Especially suited for a total weight control program requiring an anorexic is an effective non-amphetamine anorexic like Tenuate (diethylpropion hydrochloride N.F.).

It starts right away and keeps on working.

This is demonstrated by the results of 42 clinical studies involving 1291 patients receiving diethylpropion hydrochloride.*

At the end of 16 weeks, patients achieved an average weight loss of 16.1 pounds—and they were still losing weight at an average rate of a pound per week.*



October

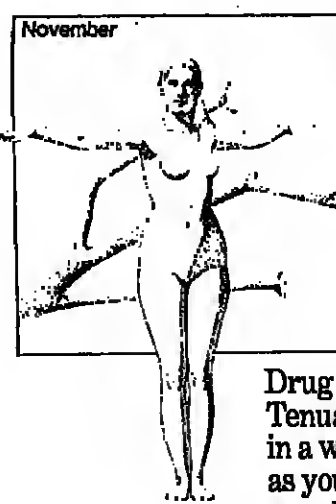
Contraindications: Concurrently with MAO inhibitors; in patients hypersensitive to this drug; in emotionally unstable patients susceptible to drug abuse.

Warnings: Although generally safer than amphetamines, use with great caution in patients with severe hypertension or severe cardiovascular disease. Do not use during first trimester of pregnancy unless potential benefits outweigh potential risks.

Adverse Reactions: Rarely severe enough to require discontinuation of therapy; un-

pleasant symptoms with diethylpropion hydrochloride have been reported to occur in relatively low incidences. As is characteristic of sympathomimetic agents, it may occasionally cause CNS effects such as insomnia, nervousness, dizziness, anxiety, and jitteriness. In contrast, CNS depression has been reported. In a few epileptic patients, increase in convulsive episodes has been reported. Sympathomimetic cardiovascular effects reported include ones such as tachycardia, precordial pain, erythema, palpitation, and increased blood pressure. One published report described T-wave

changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride; this was an isolated experience, which has not been reported by others. Allergic phenomena reported include such conditions as rash, urticaria, ecchymosis, and erythema. Gastrointestinal effects such as diarrhea, constipation, nausea, vomiting, and abdominal discomfort have been reported. Specific reports on the hematopoietic system include two cases of bone marrow depression, agranulocytosis, and leukopenia. A variety of miscellaneous adverse reactions have been



November

Generally safer than amphetamine.

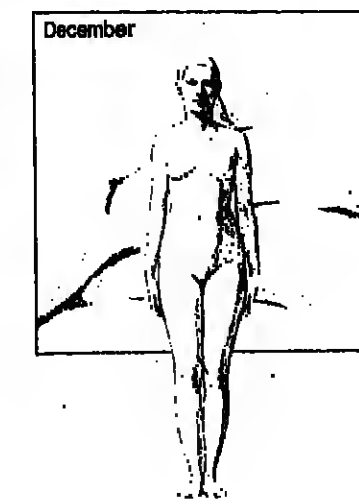
Tenuate (diethylpropion hydrochloride N.F.), a non-amphetamine, is not on the lists of drugs which come under the restrictions of the new Omnibus

Drug Bill. So you can prescribe Tenuate as adjunctive therapy in a weight reduction program as you feel necessary.

In addition, Tenuate can be used to control overweight where it complicates diabetes, hypertension, or cardiovascular

disease. (See Warning.) Tenuate can be used to help these patients because it seldom causes the excessive CNS effects associated with the amphetamines.

non-amphetamine
Tenuate
(diethylpropion
hydrochloride N.F.)



December

Wednesday, September 22, 1971

Medical Tribune

17

Ultrasound Device Detects Pre-eclampsia Better Than Nurses

Continued from page 1

nurses tended to read any difference slightly low, with a standard deviation of differences of 11 mm. Hg. compared with the physicians' standard deviation of 8 mm. Hg.

In discussing the trial, Dr. Godette said: "Although no one knows the etiology of toxemia of pregnancy, it is well established that this disease affects the vascular system early in its course and may indeed be a vascular disease. At any rate, it exhibits vascular manifestations which might be detected in the early observation of blood-pressure changes, as reflected by vascular alterations, with the use of an indirect occlusive blood-pressure measurement, relying upon the behavior of an artery as detected by ultrasonic energy."

Benign Condition Seen to Have Fatal Ability in Fibroid Case

From University of California

A "benign condition with a fatal capacity" was reported by a Los Angeles gynecologist in detailing two cases of massive fibroids.

In presenting his paper, entitled "Du Fibroids Kill?" Dr. Leroy R. Weekes, Clinical Professor of Obstetrics and Gynecology, University of California, described

the case of a widow, 59, admitted in a semicomatose, confused, and debilitated condition.

Her abdomen was markedly distended, with a large mass extending from the symphysis pubis to 6 cm. below the xiphoid process. The mass was "firm and irregular, having the physical characteristics of a massive fibroid."

The patient experienced several toxic episodes characterized by high fever, tachycardia, and ST and T-wave ECG changes, compatible with coronary artery disease.

At surgery, Dr. Weekes and his colleagues removed "a massive fibroid with tubes and ovaries which practically filled the abdominal cavity," the physician reported. "Pathologic analysis revealed many necrotic and secondarily inflamed myomata along with chronically infected tubes."

"It was felt," he said, in commenting on the case, "that this massive elongated and necrotic myoma was the source of the markedly septic state which threatened the life of the patient. Removal was critical and decisive."

The second case—which had a fatal outcome—was that of a pregnant woman, 28,

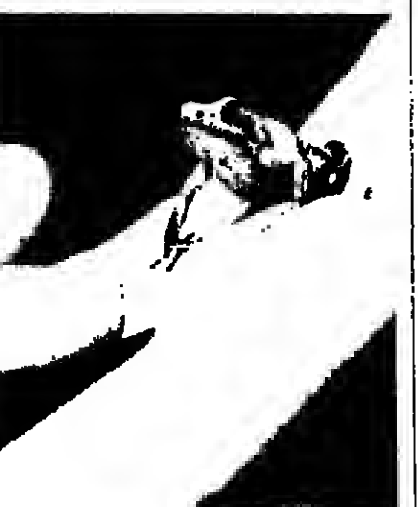
who was admitted in labor at about the 35th week of her pregnancy. Radiography disclosed "a massive soft-tissue mass resembling a fibroid filling the entire abdominal cavity." The infant was removed by cesarean section "with some difficulty" because of the many massive subserous fibroids in the lower and upper segments of the uterus. The patient's condition deteriorated postoperatively, and at surgery undertaken to remove the mass in the abdomen and pelvis, she died of cardiac arrest.

The principal diagnosis in this case, said Dr. Weekes, was "infarcted leiomyomata of the uterus with pelvic peritonitis and intestinal obstruction (paralytic ileus)."

"Although the benign nature of fibroid has long been established and need not be challenged here," the physician commented, "there must be concern about the massive grotesque fibroid which becomes a clinical problem because of its inherent size and pressure changes on contiguous organs, the lower in particular."

He noted that the "sheer size of both of these tumors was so marked that they caused pressure on the bowel [leading to] obstruction." An additional hazard of such tumors, Dr. Weekes said, is that they may undergo changes due to infection in

Frog Aids Nerve Study



Colombian Kokoi frogs, whose skin contains one of the most toxic poisons known, batrachotoxin, are part of research on electric activity of nerves and ionocytes at National Institute of Arthritis and Metabolic Diseases. Aim is to resolve frog's venom resistance.

patients with endometriosis. With extension of infection to the tumor, the entire peritoneal cavity may become involved, "as they did in both cases."

"Definitive treatment," he concluded, "should be directed in these massive tumors, whether it be myomectomy or hysterectomy, before it is complicated by degeneration, infection, intestinal obstruction, or pregnancy."

Early Therapy Urged For Hypothyroidism

Medical Tribune Report

ATLANTIC CITY, N.J.—More evidence in favor of the earliest possible treatment of congenital hypothyroidism was reported by University of Pittsburgh investigators, who believe the incidence of the myxedematous form of the disease is high enough to warrant neonatal screening programs.

The report was presented here at a joint session of the Society for Pediatric Research and the American Pediatric Society. Dr. Alan Klein and associates studied Stanford-Binet Intelligence test results at the age of three in four different groups of congenital hypothyroidism whose treatment had begun before the age of three months, three to four months, five to six months, or after six months.

While the data were variable and the standard deviations were large, the average I.Q. (89) of children treated before three months was significantly better than in any of the other groups, which averaged 70, 71, and 54, respectively.

The authors, also including Dr. Stephanie Melzer and Frederic M. Kenny, said the clinical picture in ophthalmoscopy is not usually obvious at three months, when treatment would best begin.

Grant Backs Study of Problems Due to Forestalling of Death

Medical Tribune Report

HASTINGS-ON-Hudson, N.Y.—The New York Foundation has announced a \$25,000 grant for a study of the now not urgent problems caused by man's growing ability to forestall death.

The grant will support a year's work of the Task Force on Death and Dying, one of several research panels of the Institute of Society, Ethics, and the Life Sciences.

Cochairmen of the task force are Drs. Leon R. Kniss, executive secretary of the National Academy of Sciences' Committee on the Life Sciences and Social Policy, and Eric J. Cassell, Associate Professor of Medicine at Mount Sinai School of Medicine.

Chess Solution

From the position Black forced the win of at least the exchange with the surprising 1... B-Q6!!, threatening both... BxB and... QxR.

Merrell

Parkinson Effects Relieved By Amantadine Hydrochloride

Medical Tribune Report
ATLANTIC CITY, N.J.—Amantadine hydrochloride ameliorated drug-induced parkinsonian symptoms in nine of 10 psychiatric patients with minimal side effects and no adverse effect upon the patients' mental status, according to Drs. John T. Kelly and Faruk S. Abuzzahab, of the University of Minnesota Medical School.

During a seven-day trial, the drug was most effective against akathisia and dystonia, commonly the most difficult to treat of drug-induced extrapyramidal symptoms, they told the 72nd annual meeting of the American Society for Chemical Pharmacology and Therapeutics here.

The subjects were adult hospitalized patients, six with moderate, three with marked, and one with severe psychosis, all exhibiting typical extrapyramidal side effects of rigidity, tremor, dystonia, and akathisia while taking neuroleptic medication.

Four of the patients received 100 mg. amantadine per day, and six received 200 mg. Most patients promptly responded with reduction of symptoms, both subjectively and objectively, Drs. Kelly and Abuzzahab said.

Effect Marked in Five

The therapeutic effect of amantadine was judged to be marked in five patients, moderate in four, and minimal in one. Most of the residual symptoms occurred in patients receiving unusually high doses of neuroleptic drugs.

Amantadine was discontinued in two patients early in the study, in one because of a generalized urticarial reaction that had been minimally present prior to the administration of amantadine, and in the other because of unyielding psychotic symptoms that necessitated daily increases in neuroleptic drug dose. The latter pa-

tient had a good initial response to amantadine, but symptoms re-emerged as the dose of amantadine was kept constant and the neuroleptic was increased.

Mental confusion and toxic psychosis, such as have sometimes been reported with therapeutic doses of the commonly used antiparkinsonian drugs, were not observed in this study, but this may have been related to the fact that the patients were receiving antipsychotic medications, the physicians said.

Cirrhosis of Liver Patients Aided by Kanamycin

Both oral and parenteral kanamycin led to decreased blood and urine ammonia and urino amino acids in 14 patients with cirrhosis of the liver, reported Dr. Thomas F. Nelson, Jr., D. Carlo E. Grossi, and Bo Pritz, Ph.D., of St. Vincent's Hospital and the New York University School of Medicine. No change was seen in the patients' mildly elevated plasma amino acids, however, they said.

Four of the patients were studied before and after shunt, and 10 had chronic hepatic encephalopathy. The antibiotic was given orally for three days, followed by a rest period, then intramuscularly for three days.

Six of the 10 patients with chronic hepatic encephalopathy improved on intramuscular kanamycin.

Decreased amino acid loss in urine suggests a beneficial effect on the turnover of amino acids in the liver, the investigators declared. They postulated that parenteral antibiotics may limit bacterial growth in intestinal lumen.

There is a need for reappraisal of possible beneficial effects of parenteral antibiotics in amino acid metabolism in cirrhosis of the liver, they concluded.

Physician's Aid For Parents of The Handicapped

Medical Tribune Report
MIAMI, FLA.—The physician who must break the news to parents that their baby is handicapped can provide more effective and compassionate counseling if he understands the complex emotions aroused by this situation, a British medical educator said here at an international symposium on "The Ecology of the Child and Human Development."

Dr. Ronald MacKeith, of Guy's Hospital, London, pointed out that two parental reactions must be recognized as basic and biologic—an urge to protect the helpless infant and on the other hand a feeling of revulsion at the abnormal.

The first of these is accepted while the second is frowned upon in our present culture, he told the symposium, which was presented by the University of Miami Mailman Center for Child Development. Yet revulsion is equally normal biologically, he emphasized, "and the doctor will not be judgmental when he observes it."

In Dr. MacKeith's experience, a number of other emotional states can be expected in parents who learn that their child is handicapped:

- Feelings of inadequacy about reproductive competency. These can be "deeply disturbing," particularly if the abnormal child is a firstborn. Parents see themselves as having failed once, hence the fear of recurrence "must always be ventilated, whether or not the parents themselves open the topic."

- Feelings of inadequacy in rearing the child. Like many mothers of normal first-born children, the mother of a handicapped child may worry about her competency to provide care.

- Feelings of bereavement, with attendant emotions of anger and grief. Parents have lost "the expected, lovable, ordinary child" and possibly the child they had hoped would fulfill their own frustrated desires for achievement.

Anger at such bereavement—while not always acknowledged—can be directed at "Fate, God, or the doctors," and may be combined with the protest: "Why should this happen to me?"

- Shock and surprise. Combined with these emotions may be a sense of helplessness akin to the helplessness of grief. And some parents will react by feeling that "this can't have happened—I may wake up tomorrow and find my child is normal."

- Guilt, often as a feeling of personal responsibility for what has gone wrong. There can also be overtones of conscience, with a sense of being punished.

A special burden exists for the parent who passed on a dominantly transmitted defect, but even if the disorder is inherited recessively, and both parents contributed a deleterious gene, "all too often" one parent—usually the mother—believes she is at fault.

- Embarrassment. Its intensity varies according to how dependent the parents may be on approval of other people and according to the kinds of reactions displayed by friends and neighbors.

Each of these feelings can evoke a spectrum of behavior patterns in the parents of the handicapped child, Dr. MacKeith noted. Thus, the biologic protective feeling may lead the mother to provide "usually lavish" care, while revulsion for the abnormal may show itself either as coldness or as "dull" care so intensified by guilt and overcompensation that it becomes lavish.

Dr. MacKeith cited other easily traceable patterns of behavior: gaelic anxiety and lack of self-confidence, the "coercive driving energy" of some parents' groups devoted to a particular handicap, depression, apathy, refusal to believe the doctor's diagnosis, avoidance of social contacts.

Ingredients: An homogenized, modified milk product specifically prepared for active growing babies 4 months or older. Made from water, nonfat milk solids, sucrose, corn oil, soy protein isolate, carrageenan, mono- and diglycerides, lecithin, ascorbic acid, ferrous sulfate, niacin, vitamin B₁₂ concentrate, calcium pantothenate, d-alpha tocopheryl acetate, copper sulfate, pyridoxine, riboflavin, thiamine, vitamin A palmitate, potassium iodide, folic acid, and vitamin B₆. Artificial flavors added.

Approximate Analysis	w/v per liter
Protein	36.1 gms
Fat	18.5 gms
Carbohydrate	66.1 gms
Calcium	1000 mgs
Phosphorus	400 mgs
Magnesium	85 mgs
Sodium	400 mgs
Iron	18 mgs
Copper	1 mg
Iodine	0.1 mg
Vitamin A	3000 USP units
Vitamin D	400 USP units
Vitamin E	6.25 IU
Vitamin C	50 mgs
Vitamin B ₁	0.75 mgs
Vitamin B ₂	0.90 mgs
Niacin	10 mgs
Vitamin B ₆	0.70 mg
Pantothenic acid	5.0 mgs
Folic acid	0.10 mg
Vitamin B ₁₂	2.50 mcgs
Calories per fluid ounce	16.5



Each quart provides the following percentages of vitamins and minerals needed by babies from 6 months to 2 years of age.

Vitamins and Minerals	% of RDA*
	6 mos. to 1 yr. 1 to 2 yrs.
Vitamin A	200 150
Vitamin D	100 100
Vitamin E	125 63
Vitamin C	140 125
Vitamin B ₁	150 125
Vitamin B ₂	150 150
Niacin (mg equiv.)	210 210
Vitamin B ₆	175 140
Folic acid	100 100
Vitamin B ₁₂	125 125
Calcium	170 140
Phosphorus	180 115
Magnesium	120 85
Iron	120 120
Iodine	220 180

*Recommended Daily Dietary Allowances (National Academy of Sciences)
TM-Trademark

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Now a new advance in nutrition

New Similac[®] ADVANCE[™] when formula feeding stops

The logical nutritional step after formula feeding ends is new Similac ADVANCE. It is more than a feeding, it's a whole new concept of infant nutrition. Similac ADVANCE fills the gap that has long existed between the formula feeding period and the time that solid foods alone could meet nutritional needs.

When you specify Similac ADVANCE for the post-formula feeding along with the usual solid food diet, you satisfy mother's need to change feeding without sacrificing nutrition. Similac ADVANCE is in ready-to-feed form, as convenient to use as milk, but unlike milk, it does not require refrigeration until the can is open.

6 reasons why new Similac ADVANCE is the better way to feed older babies.

(1) Because ADVANCE has less fat, more polyunsaturated fat.

The fat level in Similac ADVANCE is adjusted to 1.65% vs. 3.7% in whole cow milk and 2.0% in skim milk products. The fat ratio in Similac ADVANCE is 85% unsaturated to 15% saturated vs. 30% unsaturated and 70% saturated in whole cow milk.

(2) Because ADVANCE has fewer calories permitting weight management when indicated.

Ounce for ounce, new Similac ADVANCE contains about 20% fewer calories.

ories than either whole milk or infant formula. Excess caloric intake in the first year may set the stage for later patterns of obesity. If a baby's intake of Similac ADVANCE is no greater than that of infant formula, weight management is easily accomplished.

(3) Because ADVANCE has a delicious French vanilla flavor.

The good taste of new Similac ADVANCE assures infant acceptance. In fact, it is a good beverage for older children who refuse milk.

(4) Because ADVANCE has a growth supporting level of protein.

The protein level in new Similac ADVANCE is similar to that of whole cow milk, but there are extra advantages. In Similac ADVANCE heat treatment of the protein makes it more easily digested and reduces the likelihood of allergic reaction to milk protein.

(5) Because ADVANCE is fortified with essential vitamins and minerals.

Every liter of new Similac ADVANCE provides 100% or more of recommended daily allowances for essential vitamins and minerals. Extra vitamin supplements need not be used—a saving to the mother.

(6) Because The American Academy of Pediatrics recommends

that all bottle fed babies receive a modified milk product fortified with iron for at least the first 12 months of life.

New Similac ADVANCE is heat treated and fortified with 18 mgs of iron—a product designed to meet the latest concepts of infant nutrition.

New Similac[®] ADVANCE[™] when formula feeding stops



Women will be grateful

Pregnancy can be trying enough without the added burden of constipation. And the eeriness of the postpartum days shouldn't be marred by constipation and enemas.

That's why women are so grateful for the gentle, predictable relief you can provide with SENOKOT Tablets/Granules—the unique, colon-specific neuromuscular stimulant that can take el bedtime to induce comfortable evacuation in the morning.

You can depend on this clinically established laxative. Satisfactory evacuation with routinely administered SENOKOT preparations was achieved in 95.5% of 5,873 postpartum, pregnant, and gynecological patients. And only 3.2% of 5,827 postpartum patients were given enemas.*

High rate of patient acceptance, as well as high efficacy, may explain why SENOKOT Tablets/Granules is the leading laxative in obstetrical and gynecological practice today.

*Biotherapy available on request.

Senokot

(standardized same concentration)
Tablets/Granules
Purdue Frederick

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all in the same boat many hypertensives do better on

Esimil

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Esimil may get things moving for all sorts of patients with moderate to severe hypertension. Often controls blood pressure when other antihypertensives fail. Usually keeps it controlled, too.

The key is guanethidine—perhaps the most effective antihypertensive available.

And with Esimil, dosages of both components—guanethidine and hydrochlorothiazide—are lower than with either used alone. So adverse reactions are usually minimized. Esimil. A smoother course for all sorts of hypertensives.



Esimil
guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Indications

Hypertension (other than labile forms) which cannot be adequately controlled with simpler agents; moderate to severe hypertension associated with atherosclerosis, coronary artery disease, or progressive hypertensive disease, when side effects of other antihypertensives prevent effective treatment.

Contraindications

Guanethidine: Proven or suspected pheochromocytoma; hypersensitivity to guanethidine. Do not use with MAO inhibitors. Hydrochlorothiazide: Anuria; discontinue drug if renal shutdown occurs for any reason. Progressive hepatic disease may accelerate development of hepatic coma. Do not give to patients with known allergy to thiazides or other sulfonamide-derived drugs.

Warnings

Guanethidine and hydrochlorothiazide are potent drugs and can lead to disturbing and serious clinical problems. Physicians should be familiar with both drugs and their combination before prescribing, and patients should be warned not to deviate from instructions.

Guanethidine: Warn patients about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with head of bed elevated or head down for 15 minutes after each dose. During initial dosage adjustment and with weather changes, postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking guanethidine.

Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression. If possible, withdraw therapy 5 weeks prior to surgery to avoid possible vascular collapse and to reduce risk of cardiac arrest during anesthesia. If emergency surgery is indicated, administer pressor agents and anesthetic agents cautiously in reduced doses with oxygen, atropine, and vasopressors ready for immediate use. Give vasopressors with extreme caution because patients on guanethidine may have a greater propensity for cardiac arrhythmias. Fabrice illness may reduce dosage requirements. Due to enhanced cardiac depression and increased responsiveness to norepinephrine, special care is required when treating patients with a history of

bronchial asthma, since the condition may be aggravated.

Hydrochlorothiazide: Small bowel stenosis, with or without ulceration, has been associated with use of enteric-coated thiazides with potassium, and with enteric-coated potassium salts. These bowel lesions have caused obstruction, hemorrhage, and perforation surgery was frequently required and deaths have occurred. Although the incidence of these lesions is low, and a causal relationship in man has not been definitely established, enteric-coated potassium salts have been implicated. Therefore, enteric-coated potassium-containing formulations should be used only when dietary supplementation is not practical and discontinued immediately if abdominal pain, distention, nausea, vomiting, or GI bleeding occurs.

Lowering of blood pressure in hypertensive patients may sometimes result in nitrogen retention. In those with impaired renal function, if progressive renal insufficiency is observed, discontinuance of drug may be desirable. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects may develop in those with impaired renal function. Dosage should always be carefully titrated.

Pay special attention to electrolyte balance of patients with severe hepatic insufficiency. In patients with cirrhosis and ascites, watch for symptoms of impending hepatic coma (confusion, drowsiness, tremor) and last for increased arterial ammonia concentration, sodium and potassium. Thiazides may decrease plasma glucose tolerance use cautiously in diabetics. Hypertension may occur but is generally reversed by a uricosuric agent.

Thiazides may decrease arterial responsiveness to norepinephrine and increase responsiveness to atropine. If possible, withdraw therapy 2 weeks prior to surgery. Hypertensive episodes under anesthesia have been observed. If emergency surgery is indicated, pressor agents and anesthetic agents should be administered in reduced dosage. The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma.

since this drug crosses the placental barrier and appears in breast milk and may result in fetal hyperbilirubinemia, thrombocytopenia, or altered carbohydrate metabolism. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

Precautions

Guanethidine: Give cautiously to patients with severe coronary insufficiency, recent myocardial infarction, or cerebrovascular insufficiency. Give Esimil with extreme caution to those with severe cardiac failure.

Appetite suppressants (eg, amphetamines), mild stimulants (eg, amphetamines, methylphenidate), and tricyclic antidepressants (eg, amitriptyline, doxepin) may decrease the hypotensive effect of guanethidine. Well one week after discontinuing MAO inhibitors before starting guanethidine.

Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver function tests are advised during prolonged therapy. **Hydrochlorothiazide:** Perform serum potassium, BUN, uric acid, and blood sugar tests prior to therapy and at appropriate intervals during therapy.

Watch patients for clinical signs of fluid or electrolyte imbalance (hypokalemia, hyponatremia, alkalosis, hypocalcemia). Warning signs: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, dizziness, tachycardia, GI disorders, and uric acid. Urine electrolyte determinations are particularly important when patients are vomiting excessively or receiving parenteral fluids, or when on ACTH during brisk diuresis, or in presence of severe cirrhosis.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis may exaggerate the effects of hypokalemia, especially with reference to myocardial activity. (Signs of digitalis intoxication may be produced by therapy with thiazides.) In patients with hypokalemia or potassium-rich foods. Supplemental potassium is indicated when serum potassium is less than 3 mEq/liter or if patient is receiving digitalis. Chloride deficit may be corrected with ammonium chloride (causal in those with hepatic or renal disease) and largely prevented by a non-ionic salt intake. If dietary salt is unduly restricted, especially during hot weather, in severely debilitated patients with congestive heart failure or renal disease, a low salt syndrome may complicate therapy with thiazides.

diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide therapy.

Adverse Reactions

Guanethidine: Frequent reactions due to sympathetic blockade—dizziness, weakness, lassitude, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions—inhibition of ejaculation, fluid retention, edema, congestive heart failure. Less frequently—asthma, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, plethoric of the face, blurring of vision, peritenderness, myalgia, muscle tremor, mental depression, chest pains (angina), chest parasthesias, nasal congestion, weight gain, and asthma in susceptible individuals.

Hydrochlorothiazide: Gastrointestinal—nausea, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestasis), pancreatitis, hyperglycemia, glycosuria. Central nervous system—dizziness, vertigo, paresthesias, headache, xanthopsia. Dermatologic—hypersensitivity—purpura, photosensitivity, rash, urticaria, necrotizing angitis. Hematologic—leukopenia, thrombocytopenia, agranulocytosis, epistaxis, anemia. Cardiovascular—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Miscellaneous—muscle aches; weakness, restlessness. When severe adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

Dosage

Optimal dosage must be determined for each individual. Note: 10 mg guanethidine monosulfate present in Esimil is equivalent to 4 mg guanethidine sulfate USP (Tarnalene®).

How Supplied

Tablets (white, scored), each containing 10 mg guanethidine monosulfate and 25 mg hydrochlorothiazide, bottles of 100. Before starting therapy, consult complete product literature.

CIBA Pharmaceutical Company Summit, New Jersey

CIBA

Medicolegal Report

Sterilization Operation Ruling Is Reversed by Appeals Court

Medical Tribune Report

CINCINNATI—In a suit against a physician for alleged negligence in the performance of a sterilization operation, the highest court of Kentucky has ruled that the statute of limitations does not begin to run until the date of discovery of pregnancy.

The physician performed a sterilization operation in September, 1966, according to a report on the case by the office of the general counsel of the American Medical Association, here. The woman became pregnant in November, 1967, the pregnancy was discovered in January, 1968, and the child was born the following August.

In November, 1968 the negligence suit against the physician was filed by the woman and her husband, seeking damages for medical expenses, loss of consortium, and the expenses of raising the child to majority. The trial court dismissed the suit, ruling that action was barred by the one-year statute of limitations.

On appeal, the judgment of the trial court was reversed on the ground that the cause of action did not accrue until discovery of the pregnancy. (*Tonkinson v. Stahl*, 459 S.W.2d 166 [Ky. Ct. of App., June 5, 1970; rehearing denied, Nov. 27, 1970].)

Standard of Care for Specialist

In another case, the highest court of Michigan ruled that the standard of care for a specialist is not governed by geographic conditions but by the reasonable practice of medicine in the light of present-day scientific knowledge.

The trial court, in an action against two pediatricians for alleged malpractice in failure to timely diagnose PKU, had overruled the jury verdict of \$80,000 and granted the pediatricians' motion for judgment, holding that two of the expert witnesses who had testified against them were not competent on standards of care in the locality in question.

One of these witnesses, a world-renowned expert on PKU, testified that medicines and diets were available for treatment of the child and that it was established standard for a board-certified pediatrician to perform the tests that, he said, were routine in hospitals across the nation. Another recognized expert on PKU also testified that a test for PKU should have been made in evaluating a mentally retarded child, and also testified on the standard of care in communities similar to the pediatrician's.

Three physicians, testifying for the pediatricians, said it was not common prac-

tice for pediatricians in that area to test for PKU at that time, although they admitted that most pediatricians knew of the disease and of available treatment.

On appeal, the court said that the considerations that allowed the area practice to set the standard for general practitioners were not relevant to metropolitan specialists. (*Naccarato v. Grob*, 180 N.W.2d 788 [Mich. Sup. Ct., Nov. 12, 1970].)

Doctor-Patient Privilege

A Federal trial court in Mississippi held that the physician-patient privilege does not apply to a physician who examines an injured person at the request of the person being sued.

A man who had brought suit for personal injuries was examined by a neurosurgeon chosen by the person sued, whose attorneys then sought to take the neurosurgeon's deposition. The injured person objected, claiming the physician-patient privilege.

The court ruled that the privilege did not apply, noting that it is largely a crea-

Newly Found Infectious Particle



Newly identified plant pathogen—80 times smaller than any known virus—may shed light on human diseases such as multiple sclerosis, infectious hepatitis, and some types of cancers, stresses its discoverer, Theodor Diener, Ph.D., of the U.S. Department of Agriculture. Above, in procedure to isolate "viroid," Dr. Diener (r.) and technician Dennis Smith load nucleic acid into tube during electrophoresis test.

ture of state statute, and that there is no federally created physician-patient privilege. Privilege attaches only in a patient's own physician, the court reasoned. According to its interpretation, the rule that permits the physical examination of an injured litigant also permits calling the examining physician as a witness. (*Hardy v. Riser*, 309 F. Supp. 1234 [D. C., Miss., Feb. 9, 1970].)

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from hyperacidity



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- Oct. 22-30 ... American Society of Clinical Pathologists, Boston
- Oct. 23-30 ... College of American Pathologists, Boston
- Oct. 23-28 ... National Practice Management and Investment Seminar, 45th Annual, Honolulu
- Oct. 23-27 ... Eastern Orthopedic Association, White Sulphur Springs, W. Va.
- Oct. 24-28 ... American College of Chest Physicians, Philadelphia
- Oct. 24-30 ... American College of Gastroenterology, Atlanta, Ga.
- Oct. 26-27 ... New York State Health Department, Birth Defects Institute, Second Symposium on "Hereditary and Genetic" Albany
- Oct. 27-30 ... Gerontological Society, Houston, Tex.
- Oct. 27-30 ... American Urological Association, Mid-Atlantic Section, Williamsburg, Va.
- Oct. 27-30 ... National Hemophilia Foundation, Cleveland
- Oct. 29-30 ... American Medical Society on Alcoholism, Baltimore
- Oct. 29-31 ... American Society of Therapeutic Radiologists, Phoenix, Ariz.
- Oct. 29- ... Association of American Medical Colleges, Washington
- Oct. 30 ... Society of American Family Medicine, Washington



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INDICATIONS: All cases of hypertension except the mild and the most severe.

CONTRAINDICATIONS: Reserpine: Known hypersensitivity; mental depression, especially with suicidal tendencies; active peptic ulcer; ulcerative colitis.

Hydralazine: Hypersensitivity; coronary artery disease; mitral valvular rheumatic heart disease; hepatic disease; allergy to thiazides or other sulfonamide-derived drugs.

WARNINGS: Reserpine: Withdraw reserpine 2 weeks before surgery. If possible, for emergency surgical procedures, give vagal blocking agents parenterally to prevent or reverse hypotension and/or bradycardia.

Electroshock therapy should not be given to patients receiving rauwolfia preparations, since severe and even fatal reactions have been reported. Discontinue for 2 weeks before giving electroshock therapy.

Hydralazine: Hydralazine, particularly if given for prolonged periods, may produce an arthritis-like

syndrome, leading in rare instances to a clinical picture simulating acute systemic lupus erythematosus. Most of these reactions are reversible upon withdrawal of therapy. These side effects are not anticipated even with maximal recommended dosage of Ser-Ap-Es.

Hydrochlorothiazide: Small bowel stasis, with or without ulceration, has been associated with use of enteric-coated thiazides with potassium. Use of enteric-coated potassium alone. Coated potassium should be used only when dietary supplementation is not practical and discontinued if gastrointestinal symptoms arise.

Pay special attention to electrolyte balance of patients with severe renal or hepatic insufficiency. In patients with cirrhosis and ascites, watch for symptoms of impending hepatic coma. Thiazides may decrease glucose tolerance; use cautiously in diabetics. Hypotension may occur but is generally reversed by a urticaria agent. Lowering of blood pressure may sometimes result in impaired renal function. Dosage titration is necessary in such patients.

Thiazides may decrease arterial responsiveness to norepinephrine and increase responsiveness to tubocurarine. If possible, withdraw therapy 10 weeks prior to surgery. Hypotensive episodes under anesthesia have been observed. If emergency surgery is indicated, preanesthetic and anesthetic agents should be administered in reduced dosage.

The possibility of sensitivity reactions should be considered in patients with a history of allergic bronchial asthma.

Use in Pregnancy: Reserpine: The safety of rauwolfia preparations for use in pregnancy or lactation has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.

Hydralazine: Although there has been no adverse experience with hydralazine in pregnancy, there have been no systematic animal reproduction studies to support the idea of safety in pregnancy. The drug should be used in pregnancy only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.

Hydrochlorothiazide: Thiazides should be used with caution in pregnant or lactating patients since this drug crosses the placental barrier and appears in breast milk and may result in fetal hyperbilirubinemia, thrombocytopenia, or altered carbohydrate metabolism. It is therefore possible that the adverse reactions seen in the adult may occur in the newborn.

PRECAUTIONS: Reserpine: Use cautiously in patients with history of peptic ulcer, ulcerative colitis, or other GI disorders. May precipitate biliary colic in patients with gallstones.

Discontinue at first sign of mental depression, keeping in mind possibility of suicide. Use with extreme caution in those with history of mental depression. Take special care with asthmatics and in hypertensives with renal insufficiency. Use cautiously with digitalis, quinidine, and guanethidine. Not recommended for aortic insufficiency.

Hydralazine: Use cautiously in suspected coronary artery disease, cerebral vascular accidents, and advanced renal damage.

Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an encephalopathy affect and addition of pyridoxine to the regimen if symptoms develop.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts and liver function tests are advised during prolonged therapy.

Hydrochlorothiazide: Monitor indicated blood chemistry and fluid and electrolyte balance carefully in patients on thiazide therapy, especially when patient is receiving parenteral fluids, steroids, or digitalis. Supplemental potassium and nonrigid salt intake will help prevent hyponatremia, hypochloremic alkalosis, and hypokalemia.

ADVERSE REACTIONS: Reserpine: Increased salivation, increased gastric secretions, nausea, vomiting, anorexia, aggravation of peptic ulcer or ulcerative colitis, increased intestinal motility, diarrhea, engine-like syndrome, ectopic cardiac rhythms, particularly when used concurrently with digitalis, bradycardia, flushing, and mental depression, drowsiness, lassitude, nervousness, periorbital edema, nightmares (which may be an early sign of mental depression), rarely atypical Parkinsonian syndrome, central nervous system sensitization (manifested by dull sensorium, deafness, gliucoma, uveitis, and optic atrophy), pruritus, skin rash, dryness of mouth, dizziness, headache, syncope, epistaxis, purpura due to thrombocytopenia, asthma in susceptible persons, nasal congestion, weight gain, impotence or decreased libido, enhanced susceptibility to colds, dysuria, conjunctival injection, dyspnea, muscular aches.

Hydralazine: Common: Headache, palpitations, anorexia, nausea, vomiting, diarrhea, tachycardia, angine pectoris.

Less frequent: Nasal congestion; flushing; lacrimation; conjunctivitis; paresthesias; edema; dizziness; tremor; muscle cramps; psychomotor reactions characterized by depression, disorientation, or anxiety; hypersensitivity reaction including skin rash and vascular collapse; constipation; difficulty in micturition; arthralgia; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly.

Hydrochlorothiazide: Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis, hyperglycemia, glycosuria, dizziness, vertigo, paresthesias, headache, xanthopsia, purpura, photosensitivity, rash, urticaria, necrotizing angitis, leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia, muscle spasm, weakness, restlessness. Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

DOSAGE: One or 2 tablets t.i.d. To initiate therapy, 1 tablet t.i.d. is recommended. For maintenance, adjust dosage to lowest patient requirement. When necessary, more potent antihypertensives may be added gradually in dosages reduced by at least 50 percent.

SUPPLIED: 7 tablets (salmon pink, dry-coated), each containing 0.1 mg reserpine, 25 mg hydralazine hydrochloride, and 15 mg hydrochlorothiazide; bottles of 100 and 1000.

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C I B A

Wednesday, September 27, 1971

Odds and Ends

• "The husband who needles and berates his wife for being fat may be the main reason she became, and stayed, that way," says a release from the University of Michigan.

It goes on to report that a professor at the university's School of Social Work has discovered that some husbands want their wives fat to keep them from promiscuity, or because they think it's attractive, or for "personal oncupmanship." We assume these husbands are not the needlers and beraters but confess in a certain amount of confusion.

This confusion mounts to a peak at the end of the release with the statement that the professor "has been 85 per cent successful with married women, compared to 30 per cent success with unmarried." The husband's assistance in managing his wife's eating behavior has been a big factor in the diet's results," he observes. "Men control their wives' weight."

Oh well, that reducing business never was simple!

• The anonymous contributor from West Virginia University Medical Center has sent us, from an unnamed source, the following notice:

"The Florida Advisory Group adopted unanimously a motion commending work of the Florida Regional Medical Program staff in connection with the developing FAG activities."

• The chief copy editor has called our attention to Webster 11's definition of "ugliness": to wit: "adj. [see ug; 1st-some.] Horrible. Archaic."

Naturally, we went to see ug and found "n. a feeling or object of disgust."

He says that ug is handy to have around for Scrabble, and we think it's helpful, as a safety valve, while reading newspapers.

• Science turns up in odd places, but *Nature* has located one of the oddest: the back of Nicaraguan postage stamps.

We gather that the Nicaraguan government has issued a series of 10 stamps to commemorate "the 10 mathematical equations that changed the face of the Earth." The face of the stamp states and illustrates the equation; an explanation of it appears on the back.

The cheapest equation (oo the 10-centavo stamp) is $1+1=2$, *Nature* reports; for twice that, you can get $e=mc^2$; and for a two-córdoba airmail stamp, you get the most expensive: Napier on logarithms or the Maxwell equation, whatever either of them may be.

• We pass on, for what it's worth, the following news from a Harvard University press release:

"The man-on-the-street thinks achievements of modern technology such as television, computers, and automation are good for him, but he is doubtful about the benefits of the space program. He believes there is such a thing as the military-industrial complex, but he doesn't know what it consists of."

We wonder what street the investigators were on.

• We've just discovered that proctology has a patron saint: Saint Flaccus.

Not surprisingly, our source is the *American Journal of Proctology* which reports: "... on the one hand he was the protector of gardens and on the other hand he was also the healer of all intestinal affections and hemorrhoids."

• A letter to the editor of the *New England Journal of Medicine*, birthplace of the Chinese restaurant syndrome, offers the Japanese restaurant syndrome.

Readers are invited to contribute items of 100 words or less to this column. Contributions should be mailed to **MINICAL TALKERS**, 110 East 59th St., New York, N. Y. 10022.

A Warning to Young Swimmers On Underwater Competition

Medical Tribune Report

NEW YORK—A warning that children should not be permitted or encouraged to engage in competitive underwater swimming under any circumstances because of the extreme perils of possible hypoxia was voiced here by Dr. Albert B. Craig, Jr., Associate Professor of Physiology at the University of Rochester School of Medicine and Dentistry.

"Loss of consciousness during underwater swimming can occur when the swimmer is trying to set a record for distance or time," he told a meeting held by the Committee on the Medical Aspects of Sports of the Medical Society of the State of New York.

"Invariably, the subject voluntarily hyperventilates before the swim. Loss of consciousness occurs with little or no warning and the subject may continue to swim for a time despite such loss. People watching often do not realize that the swimmer is in trouble until final collapse."

Death is a common result," he stated.

Dr. Craig explained that if a swimmer's breath hold is done following normal respiration, the partial pressure of carbon dioxide increases to the point at which he can no longer resist the urge to breathe again. In other words, he has reached "the breaking point."

"This breaking point signal," he continued, "occurs even if he is exercising. Under these conditions the partial pressure of oxygen decreases but does not get to levels which are dangerous. On the other hand, if the subject hyperventilates and 'blows off' the carbon dioxide before the breath hold, the increase of the carbon dioxide during the breath hold is slower and the breath-holding ability is increased."

"Under these conditions, the 'breaking point' may not be reached before the partial pressure of oxygen decreases to a dangerously low value. When exercise is continued with the breath hold following hyperventilation, the partial pressure of

oxygen decreases even faster and hypoxia is quite easy to produce. The subject can pass out even without feeling the urge to breathe again. This type of loss of consciousness, due to hypoxia, occurs with little or no warning, and until the final moment of complete collapse the subject may continue what he is doing."

Dr. Craig cited 52 cases of loss of consciousness while swimming, all of whom were in the 12- to 33-year age range with most between 16 and 20 years old. Only two of the victims were girls. Thirty-six of 46 cases in which the location of the accident was known occurred in guarded pools. There were 21 deaths in the series.

He stressed that loss of consciousness while swimming under water is preventable if people are taught to swim under the surface of the water as they are taught to swim on the surface. Furthermore, swimmers should be cautioned not to attempt to establish records for time or distance and should know that hyperventilation enhances the danger of loss of consciousness.



DR. CRAIG



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